U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-245 023

EVALUATION OF THE POSSIBLE IMPACT OF PESTICIDE LEGISLATION ON RESEARCH AND DEVELOPMENT ACTIVITIES OF PESTICIDE MANUFACTURERS

ARTHUR D. LITTLE, INCORPORATED

PREPARED FOR
ENVIRONMENTAL PROTECTION AGENCY

FEBRUARY 1975

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PB 245 023

EPA-540/9-75-018
February 1975

Evaluation of the Possible Impact of Pesticide Legislation on Research and Development Activities of Pesticide Manufacturers

Office of Pesticide Programs
Office of Water and Hazardous Materials
Environmental Protection Agency

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BIBLIOGRAPHIC DATA SHEET	1. Report No. EPA-540/9-75-018	2.	3. Recipient's Accession No.

4. Title and Subtitle
Evaluation of the Possible Impact of Pesticide Legislation on Research and Development Activities of Pesticide Manufacturers

5. Report Date
February 1975

6.

7. Author(s) Aldred E. Wechsler, Joan E. Harrison and John Neumeyer

8. Performing Organization Rept. No.

9. Performing Organization Name and Address
Arthur D. Little, Inc.

10. Project/Task/Work Unit No.

11. Contract/Grant No.
68-01-2219

12. Sponsoring Organization Name and Address
Office of Pesticide Programs, EPA, 401 M. Street, SW,
Washington, D.C. 20460

13. Type of Report & Period Covered

14.

15. Supplementary Notes
Robert E. O'Brien was the OPP Project Officer

16. Abstracts The report looks at research and development activities of pesticide manufactueres as R&D is affected by pesticide legislation. It deals with trends in the pesticide industry and the R&D process and decision making, product development, and innovation. It compares FIFRA with FEPCA and talks to both specific and general impacts of legislative and regulatory actions. It also make recommendations to reduce adverse effects of FEPCA implementation.

17. Key Words and Document Analysis. 17a. Descriptors

FIFRA
FEPCA
research
product development
decision-making
FEPCA implementation
pesticide industry
Federal Environmental Pesticide Control Act

Federal Insecticide, Fungicide, and Rodenticide Act
market factors
R&D trends
legislative actions
registration requirements
experimental use permits
restricted use/certified applicators
compensation for data
pesticide reregistration

regulatory actions
general impacts
risks in development
synthesis and screening
biological evaluation
field testing
data gathering
costs
economic considerations
pesticide

17b. Identifiers/Open-Ended Terms

PRICES SUBJECT TO CHANGE

17c. COSATI Field/Group

18. Availability Statement Available from the National Technical Information Service	19. Security Class (This Report) UNCLASSIFIED	21. No. of Pages 124
	20. Security Class (This Page UNCLASSIFIED	22. Price 5.25

EVALUATION OF THE POSSIBLE IMPACT OF PESTICIDE LEGISLATION ON RESEARCH AND DEVELOPMENT ACTIVITIES OF PESTICIDE MANUFACTURERS

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For

Environmental Protection Agency
Office of Pesticide Programs
Robert E. O'Brien, Project Officer

EPA 540/9-75-018

February 1975

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PREFACE

This report was prepared by Arthur D. Little, Inc. (ADL) under Contract No. 68-01-2219 for the Office of Pesticide Programs of the Environmental Protection Agency. The principal authors were Alfred E. Wechsler, Joan E. Harrison, and John Neumeyer (consultant to ADL). Other ADL staff contributions to the program were: Joan B. Berkowitz, Alan W. Burg, John T. Funkhouser, Janet M. Stevens, and Edward S. Shanley. The authors acknowledge the guidance and assistance of the EPA project officer Mr. Robert E. O'Brien of the Office of Pesticide Programs. The study results were made possible through the excellent cooperation and the information provided by the National Agricultural Chemicals Association and the following companies:

American Cyanamid Company
American Hoechst Corp.
Amchem Products, Inc.
Chemagro, Division of Baychem Corp.
Chevron Chemical Company
Diamond Shamrock Chemical Co.
E.I. duPont de Nemours and Company
Elanco Products Company
FMC Corporation
Gulf Oil Chemicals Company
IMC Corp.
Monsanto Chemical Products Company
Nor-Am Agricultural Products, Inc.
Nutrilite Products, Inc.
Occidental Chemical Company
Shell Chemical Company
Stauffer Chemical Company (California and Connecticut)
Union Carbide Corporation
U.S. Borax Research Corporation
Velsicol Chemical Corporation
Zoecon Corporation

This report reflects the views of the authors and their interpretation of those expressed by industry. It has not been reviewed or commented on by other parties interested in pesticides such as environmental groups, the U.S. Department of Agriculture, or the staffs of academic institutions.

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I. SUMMARY

A. PURPOSE AND SCOPE

Although the pesticide industry has developed under the constraints and benefits of federal regulation for over 25 years, new pesticide regulations promulgated under the Federal Environmental Pesticide Control Act (FEPCA) of 1972 could have a significant impact on the innovative--research and development--activities of pesticide manufacturers. Decreases in innovation would ultimately affect the type and quantity of new pesticides entering the market, would alter pesticide production and use patterns, and could increase the cost of agricultural production. These effects could be counteracted by potential improvements in safety and environmental quality and by the development of new pest control methods brought about in response to new regulations.

The purpose of this program was to examine the probable effects of past and current federal regulations on innovative research and development (R&D) activity in the pesticide industry. More specifically our goals were to:

- Describe and identify trends in key factors that influence innovative activity in the pesticide industry.
- Examine the impacts of past pesticide legislation and regulations on innovative activity in the pesticide industry.
- Assess the probable impact of recent pesticide legislation on innovative activity in the pesticide industry and suggest methods for minimizing adverse impacts.

Our work was focused on obtaining and examining industry's reactions to past regulatory activities and industry's anticipation of how recent and proposed regulations would impact future R&D activities.

B. APPROACH

The trade, scientific and regulatory literature covering the past 10 years was reviewed briefly in order to develop background information on the research and development activities of the pesticide industry. Pesticide regulations from the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) of 1947 through FEPCA were examined and compared. Discussions were held with the management, marketing, research, engineering and regulatory liaison staff of 22 companies representative of the large and small, new and old sectors of the pesticide industry that perform research and development. Information was obtained on the principal impacts of past regulations on R&D, the anticipated implementation of FEPCA and its potential impact on R&D, approaches to mitigating adverse effects of FEPCA implementation, and trends in R&D activities that demonstrated the impacts of regulations. This information, as well as additional data obtained from EPA staff, the literature and trade associations, was analyzed and integrated into this report.

C. RESULTS

1. Structure and Market Factors

Among the many U.S. companies involved in the manufacture, formulation, distribution, and sale of pesticides, the major innovative research and development efforts are conducted by about 30 organizations that manufacture pest control products. Most of these companies are multi-product firms, for which pesticides comprise less than 20% of the total sales. About 2/3 of the companies engaged in pesticide R&D are large chemical- or petroleum-based firms; several are multi-product pharmaceutical companies; the remainder are a variety of smaller firms in which pesticides comprise from 20% to 100% of all product activities. In many respects, the pesticide industry and its R&D activities are similar to the pharmaceutical industry and are characterized by:

- A high degree of federal regulation;
- Large R&D investments as a percent of sales revenues;
- Significant risk in product development, with large expenditures on unsuccessful as well as successful products;
- Extensive product screening and testing programs;
- Considerable time lag from invention to commercialization of product; and
- Competition among proprietary products of different companies.

The high risks associated with pesticide development are a result of several factors. Only about one in 7000 potential products entering the initial screening phase of R&D will result in a successfully marketed product. Others are eliminated on the basis of efficacy, safety, cost, competitiveness, or environmental factors. Because of the time lag (presently 6 to 8 years) from invention to commercialization of pesticides, additional risks are encountered because of the uncertainty of market projections, commitment of capital for facilities, commitment for raw materials, and the uncertainty of the registration process.

The highly specialized requirements for personnel (biologists, entomologists, plant pathologists) for R&D facilities (analytical laboratories, greenhouses, experimental farms) and for pilot and production facilities preclude shifts from pesticide R&D to R&D of other products.

Since large sustained commitment of resources is needed, the principal contributors to pesticide R&D are the multi-product firms with continuous income from other products. There are few new corporate entries into pesticide R&D, and there is continued management pressure to reevaluate pesticides as products, based on risk and rate of return considerations.

Among the pesticide products, herbicides have experienced the largest growth both in sales and in R&D; this trend is expected to continue. Research and development in insecticides has shifted from chlorinated hydrocarbons to organophosphates, carbamates, and more recently juvenile hormones. Directed research on fungicides is only modest because of the lower overall market potential. Research on biological approaches to pest control is also very limited.

Most pesticide R&D activities are focused on pests that attack major crops--corn, cotton, soybeans, small grains, rice and alfalfa. Because development costs for products for major crops are comparable to those for minor crops, those products with lower potential sales volume are naturally dropped.

Other market factors that affect pesticide R&D include: competition and substitutability in the herbicide and insecticide market among similar products for the same crops, foreign markets to supplement U. S. sales and production activities, government agricultural support policies which can either increase or decrease the demand for pesticides, AID and military markets, pesticide demand, and the energy and petroleum shortages.

2. Trends in R&D Activities

The pesticide research and development process consists of:

- Synthesis and screening--initial preparation of small amounts of chemicals that are screened for pesticidal activity.
- Preliminary data gathering--synthesis of larger amounts of promising chemicals for use in laboratory or greenhouse tests of toxicity, efficacy, and environmental effects.
- Experimental field use--acquisition of use permits and conduct of intensive field studies on efficacy, application rates and methods, residues, pathways and levels of ecological penetration.
- Registration--compilation of toxicity, efficacy, environmental, and product data, submission to EPA, and obtaining of a label.
- Process development and marketing--engineering design of process, pilot plant operation, plant construction, and operation.

The estimated cost for discovery and development of a pesticide is currently about $7.5 million including the costs of unsuccessful compounds. This cost has increased by over 100% since 1967, as a result of the growing sophistication of the industry, increased competition among products, and the increased costs of R&D, particularly the increased field testing. The costs of maintaining existing products has also increased. The cost for developing a single successful product has increased from about $1.0 million in 1960 to about $3.0 million in the early 1970's. Much of the R&D expenditures of pesticide companies, which average about 6% of sales are devoted to obtaining data and information for registration of new products and to the maintenance of the registrations of existing products.

The timing of the R&D process, i.e., the duration from initial synthesis to registration, has increased from about 3 years in 1960 to 4.5 years in the late 60's and to more than 7.0 years at present. Principal increases in timing have resulted from increased toxicity (carcinogenicity, mutagenicity, etc.), residue, and environmental fate tests, field tests, and the registration process itself. Similarly, manpower levels for R&D in the pesticide industry have increased by about 100% over the past 15 years as a result of toxicity, environmental and field testing, and the requirements for constant attention to regulations.

Principal factors in decision-making concerning potential products for continued R&D efforts include (in decreasing order of importance):

- Efficacy--performance in solving a particular pest problem,
- Cost in relation to existing or anticipated competitive products,
- Volume of potential market, and
- Safety and environmental factors.

The number of new pesticide products developed annually by each company has decreased by about 50% over the period from 1960 to 1970. The decrease can be traced in part to regulatory requirements associated with pesticide residues on food products. Caution by decision-makers in a high-risk business, the decreased importance of minor use markets, and the general decrease in innovative activity resulting from increased need for defensive research on existing products have also contributed. The number of product registrations per company has not decreased as significantly, a trend indicating the need to register products for as many applications as possible.

Other trends include an overall decrease in R&D on insecticides and fungicides and an increase in R&D on herbicides. In general, industry does not feel that biological control approaches are worth pursuing extensively at this time because of efficacy, cost, market volume, and safety factors.

In addition, technical difficulties in storage and stability, the lack of patent protection, and anticipated problems in user acceptance have also prevented investments in this R&D area.

3. Legislative Actions

The principal legislative actions that have affected pesticide research and development in recent years have been FIFRA (1947), the Delaney amendment to the Federal Food, Drug and Cosmetic Act (1962), the policy changes in pesticide residue requirements during 1966-67, PR Notice 70-15 (1970), FEPCA (1972) and the regulations proposed and promulgated under FEPCA since its enactment.

The data required for registration under FIFRA evolved from 1947 to 1971 at a slow, steady pace. The provisions that have had the greatest impact on pesticide R&D include:

- The data requirements for pesticide registration and labeling, for example, toxicity tests and data including safety, physical/chemical properties, efficacy, and labeling information;
- Data required for the establishment of tolerances on agricultural commodities, e.g., chemical, toxicological (acute, short-term, long-term), biochemical, reproduction studies, etc.; and
- The experimental use permit program, which required additional data and permits for field testing of potential pesticide products.

Significant step increases in the data requirements occurred as a result of the Delaney Amendment, which prohibited the occurrence of any known carcinogen in food products. Another step increase occurred as a result of the policy changes of 1966-67, which required reevaluation and reregistration of pesticides that had been previously registered with "no residue" or "negligible residue" status. These changes required additional laboratory and field testing of already marketed (and newly developed) pesticides in order to establish finite tolerance levels and to ensure that carcinogens were not present in any residue. The PR 70-15 notice posed a number of questions pertaining to the fate and significance of pesticides in the environment, questions for which extensive data had to be obtained prior to registration.

FEPCA (also referred to as FIFRA, amended) contains many new provisions and regulations that are now being implemented. Registration requirements are similar to FIFRA, although pesticides in both inter- and intra-state commerce are now covered by FEPCA. Major differences between FEPCA and FIFRA include:

- Additional data requirements to be provided with registration;
- Emphasis on demonstration that normal use of pesticides will not result in unreasonable adverse effects on the environment;
- Strengthened suspension, cancellation and enforcement procedures;
- Classification of pesticides for general use or restricted use;
- Requirements for certified applicators for restricted use pesticides;
- Provisions for compensation for the use of others' test data in support of registration applications;
- Indemnity for certain persons suffering loss as a result of suspension and cancellation of a registration;
- The establishment of storage, disposal and packaging provisions;
- An expanded experimental use permit system with additional data requirements;
- Increased responsibilities and authorities for states in regulation of sale or use of pesticides; and
- Commitment to research to aid implementation of FEPCA.

Those provisions of FEPCA that are expected to have major impacts on pesticide R&D are described further in the following report.

In parallel with these regulatory changes has been a shift in emphasis in the registration process and data requirements from efficacy and safety (when the regulations were administered by USDA and FDA) to safety and environmetal effects (under the present administration by EPA). Industry believes that this change in emphasis and accompanying attitude of the regulators has had as much impact on R&D as the regulations themselves.

4. Specific Impacts of Legislative Actions

Registration requirements--The steadily increasing requirements for data on health, safety, and environmental effects to support registration of pesticides have significantly increased the cost and time frame for pesticide registration and development by industry and have resulted in a decrease in the rate of innovative research and development activity as was discussed previously. These costs and delays have been balanced by a greater understanding of pesticide effects, derived from registration data, and by the registration of effective, safe and environmentally sound pesticides. The increase in cost and time frame for pesticide development and registration result from both technical data requirements and procedural requirements.

Industry generally accepts the fact that increased technical data are needed to provide the scientific basis for registration of pesticide products. Although there are some specific difficulties encountered in test requirements and test procedures, industry is capable of meeting technological requirements with the associated cost and time increases. Procedural problems of pesticide registration, on the other hand, occupy the concern of industry and are felt to result in unacceptable delays and costs that discourage innovative activity. Industry feels that these procedural problems could be resolved through conscientious efforts by both the regulatory agency and industry. Other impacts of increasing data requirements for registration include: earlier decision-making with respect to pursuing specific potential products, specialization by pesticide research organization in certain technical areas and use of contractor assistance in others, and additional information on pesticide fate and significance in the environment which may help prevent long-term adverse environmental effects.

Experimental Use Permits--The proposed experimental use permit system under FEPCA will increase the costs, timing, and risks in pesticide research and development activities. Industry can be expected to challenge the proposed regulations unless methods are found within the scope and intent of the permit system to obtain data on efficacy, application rates, environmental and geographic variables, and to obtain marketing information such as acceptance by the farmer, comparison with competitive products, etc. Because use permits were "easy to obtain" and because the data and information were developed for the decision-making process of pesticide development on a timely and cost-effective basis, the looseness of the regulations may have resulted in indiscretions and violations of the intent of the permit system.

Changes in the experimental use permit system proposed under FEPCA, such as the restriction on pesticide resale, limitations on exceptions to the permit system, added data needed to obtain the use permit, and procedural requirements are designed to prevent such indiscretions. These changes have been labeled an "overreaction" by industry, which predict that significant impacts on R&D will occur. Industry feels that restricting marketing data from the field permit program may hamper the decision-making process and result in the flow of fewer acceptable products to the marketplace.

Data needed to obtain experimental use permits will be required early in the screening process. At that point in time, many potential products have not been eliminated by screening; thus an increase in the cost of R&D will result. Greater staffing to manage the field program and increased facilities (experimental farms) will also increase R&D costs. The duration of the R&D process, from discovery to registration, may increase by up to 12 months. A shift in the order and scheduling of R&D activities may also occur, so that more toxicological and environmental degradation work will be required in early stages of product screening. Smaller pesticide companies may be more severely affected than large companies. The overall impact of the new experimental use permit system will decrease innovative activity on new pesticides, encourage expansion of present product lines to more applications, and result in increased R&D costs passed on to the consumer, but will provide a better control of the environmental impact from pesticide use.

Restricted Use/Certified Applicators—The restricted use classification system and the requirements for certified applicators will have little or no direct impact on R&D activities because they do not require additional data, research activities, additional R&D staff, or changes in the time frame for R&D. Industry anticipates that large numbers of applicators will be certified and that pesticide preferences and markets will still be determined by product efficacy and cost rather than use classification. Industry is uncertain as to whether the use classification/certified applicator system will aid the registration of certain products for restricted use that might otherwise not be registered.

Compensation for Others' Data--Section 3(c)(1)(D) of FEPCA dealing with compensation for the use of other companies' data in support of registration was strongly supported by industry in the legislative formation of FEPCA. This provision will probably provide administrative and procedural problems for EPA and industry but will have little impact on research and development activities.

Pesticide Reregistration--The reregistration of currently registered pesticides, as required by FEPCA, will most likely decrease innovative R&D activities by industry over the next 2-5-year period because of the anticipated additional data requirements for reregistration. These requirements are expected to catalyze the removal of presently marginally profitable pesticides, particularly those for minor crop use, from the market. Industry has given little attention to reregistration because of other more pressing problems presented by FEPCA.

Other major changes in regulations resulting from FEPCA--indemnification resulting from suspension and cancellation of pesticides, books and records requirements, enforcement procedures, intrastate coverage, pesticide disposal provisions, etc.--are expected to have little direct impact on pesticide R&D and only secondary impact through marketing and sales effects.

5. General Impacts of Regulatory Actions

The increased costs of pesticide R&D, caused partly by regulations, will probably result in an increased emphasis on short-term return on R&D investment and a decreased emphasis on effort which can bring long-term, but relatively uncertain, return. Thus, there will be increased effort to capitalize on existing products, extend product lines to new applications, and conduct defensive research on existing products. This defensive research will result in a decreased emphasis on new innovation in pest control. The projected market value of a potential pesticide product will have to be higher for the compound to be developed through the more costly R&D process. Fewer new pesticides are expected to be registered and enter the market, and potential products without a relatively certain promise of return may be "placed on the shelf." More importance will be given to international markets to bear the costs of the R&D process.

Regulations have resulted in an extension of the duration of the R&D process to about 7 or 8 years from initial synthesis to registration of a new product. Within this time period, a reordering of parts of the R&D process has occurred, so that needed environmental and toxicological data for experimental permits or for better decision-making is obtained as early as possible. The reordering of the R&D process also affects decisions for new plant construction investments, as well as for market development.

Staffing needs of companies engaged in pesticide R&D have increased; more biologists, environmental chemists, engineers, and regulatory liaison personnel are needed.

Industry has some concern over the decrease in available patent life of proprietary products brought about by the increased duration of the R&D process. However, there is more concern over the possible decrease in market share and profitability resulting from the entrance of new competitive proprietary products than over the loss of a year or more of patent life. Some form of proprietary or patent protection is especially needed in the area of biological controls to stimulate R&D activities in this area.

Regulatory actions as well as general economic considerations will decrease the number and availability of pesticides specific to minor crop use. Once a major market is developed the use of pesticides will be extended to minor crops. However, little innovative research for pest control on minor crops per se is expected to occur.

The impacts of regulatory actions--costs, timing and procedural problems--can be better absorbed by the large diversified pesticide companies than by the smaller companies involved in pesticide R&D. Thus, although the climate and potential for innovative R&D may be better in the smaller companies, the number of smaller companies conducting R&D will probably decrease. Similarly, the number of new companies entering in the pesticide R&D area will be small, because of the large and long-term commitment required before any new product can provide a reasonable return.

The impacts of regulations apply equally to biological controls as to innovative chemical pesticides. These impacts, coupled with the technical problems and limited present markets, suggest that R&D on biological control will have to be supported or subsidized by the federal government before any reasonable progress can be made in today's economic climate.

D. CONCLUSIONS AND RECOMMENDATIONS

The major conclusions developed in this study are:

1. Over the past 25 years pesticide regulations have increased slowly and steadily in breadth and depth; their impact on innovative research and development in industry has increased in parallel. Major impacts on R&D activities have already occurred prior to FEPCA as a result of the requirements for safety and environmental data. Although the implementation of FEPCA will result in additional impacts on specific portions of the R&D process, the act itself does not represent drastic changes in innovative activity.

2. The principal impacts of this steady growth in regulatory action on pesticide R&D activities include:

    - substantial increases in the time and costs of pesticide development;
    - increased risk for the pesticide developer;
    - increased allocation of R&D resources to the defense and maintenance of existing product lines and extension of pesticides to new uses at the expense of decrease in innovative R&D;
    - reordering of the timing of specific R&D activities and reallocation of some R&D manpower resources;
    - increased emphasis on development of products for foreign markets in order to increase sales volume.

3. Implementation of the registration requirements and experimental use permit system under FEPCA will result in increased R&D costs, and lengthening and reordering of the R&D tasks. Only minor impacts on R&D activities are anticipated from FEPCA provisions dealing with certified applicators, restricted use classification, compensation for data, packaging, disposal, etc.

4. The principal impacts of pesticide regulations on future pesticide product development are:

    - continued development of potentially high volume/profit compounds such as herbicides;
    - continued emphasis on products for major agricultural crops with decreasing emphasis on products for minor crops; and
    - continued decrease in the number of new pesticides which enter the marketplace.

5. The principal decision-making factors in the development of a potential pesticide product are, in order of importance:

   - efficacy,
   - projected cost compared with competitive products,
   - anticipated sales volume and profitability,
   - human safety (toxicity), and
   - environmental impact.

   Recent regulations may eventually increase the importance of environmental impact as a decision-making factor; the other factors remain more important in determining whether potential products will reach the marketplace.

6. The large, established, multi-product, diversified pesticide developers will continue to be the major source of R&D in industry since they can continue to develop and market new products, given the required time and cost investments necessary. The smaller and more recently formed companies may not be able to sustain the increases in R&D costs and extended product development time. They will either withdraw from the R&D function, be consolidated with larger companies, or withdraw from the marketplace. This will result in a decrease in innovative activity, due to the decrease in the number of companies participating in pesticide R&D.

7. Potential products based on most biological control approaches have serious technical problems, are not cost competitive, have poor anticipated acceptance by the user, and are not believed by industry to be more safe than chemical approaches. Biological controls are not expected to gain a significant market share in the near future despite the encouragement provided in recent regulations.

8. Industry has recommended ways to reduce some of the anticipated adverse impacts of FEPCA; most of these address procedural changes that will help reduce the cost and duration of the pesticide development and registration processes. Improvement of the long and inefficient registration process by EPA will remove a significant barrier to pesticide development and use. However, these procedural and registration changes, by themselves, will not significantly increase innovative pesticide research and development. Federally supported incentive programs which also eliminate other significant barriers are needed to promote innovative pesticide R&D and increase the number of new pesticides that are safe, effective and environmentally acceptable.

Principal recommendations for reducing adverse effects of regulatory action on pesticide R&D are:

1. Develop policies and procedures for improving the pesticide registration/review process at EPA:

   - publish complete registration guidelines with a balance between flexibility for different pest control approaches and specificity of detailed data requirements for all approaches;
   - develop procedures for updating registration guidelines;
   - establish definitive schedules for the registration/review process with attention given to frequent EPA/registrant communication;
   - incorporate seasonal effects of field tests and pesticide usage in the timing of registration reviews; and
   - develop procedures for consistency of internal review at EPA.

2. Develop policies and procedures for expanding and diversifying the EPA pesticide registration staff:

   - recruit staff experienced in agriculture, pest control development, health and safety, environmental effects at increased pay levels;
   - develop programs for internship/work/study of EPA registration staff at USDA, universities and industry or develop an EPA/university/industry exchange program;
   - provide for flexibility in number and experience of registration staff for peak load periods, including seasonal trends in experimental permit applications.

3. Develop policies and proceduresfor improving intra- and inter-agency communication, liaison and cooperation with EPA Criteria and Evaluation Division and Registration Division, EPA regional offices, USDA staff, state environmental and health agencies, and agricultural extension services.

4. Develop policies and procedures to enhance the implementation and benefits of the experimental use permit programs: for example, a co-monitor program for evaluation of field studies by EPA Registration Division or EPA regional staff, allow distributors and dealers to participate in the experimental use program.

5. Conduct research and communicate the results to industry in the following areas:

   - cost/benefit analyses on the decision-making factors and criteria for acceptance of toxicity and environmental impact data for pesticide product registration, suspension, and cancellation;
   - biochemical studies to elucidate mechanisms of pest control and enhance new pest control approaches;

- biological control approaches--mechanisms of action, stabilization of viruses and bacteria, application methods, and consumer acceptance;

- pesticides specific to minor crop uses;

- toxicology and environmental information on classes of chemical and biological pesticides in common use or expected to be developed.

6. Develop a broad program of incentives to foster innovative R&D activities by industry and universities. The incentives considered should include: government-funded research, government-performed research, proprietary protection alternatives, insurance incentives, R&D loan/payback systems, total integrated pest control systems, etc.

II. INTRODUCTION

A. BACKGROUND

During the past quarter century of intensive organic chemical pesticide development, many products and product forms have been placed on the market. These include all types of chemicals, the principal varieties being insecticides, fungicides, herbicides, plant growth regulators and some biological products. Modern food production and public health programs are dependent upon the use of these pest control agents. The number of people who use pesticides is increasing continuously; the number exposed to the effects of these chemicals is almost the total population. The production and use of pesticides in the United States continues to grow in response to the demands of the U. S. and foreign users. Production of some pesticides are reaching new levels, while others are being severely limited because of the substitution of new or improved chemicals or changes in U. S. and foreign markets. At the same time, concern for environmental quality has led to legislative action which may affect the present research, and development, production and use of pesticides.

The development cost for a new pesticide is influenced by a number of factors. Some are related to the nature of the chemistry of the pesticide and involve the inherent risk in developing a specific chemical ingredient with desired characteristics. In the past the most important influences on costs were those caused by the nature of our economy, i.e., labor, equipment, sales costs, facilities, overhead, etc., as well as the intended use of the new pesticide (for food crop or non-food crop). Pesticide manufacturers have been aware of the high risks and costs involved in the development of a new pesticide. Another important part of each decision to develop a new pesticide is the anticipated competitive situation in the marketplace. A new compound which has better activity, is safer, more convenient to use or less costly than competitive pesticides has economic advantages which make it attractive to the market. These factors are often unknown or difficult to determine in the early stages of product development. If adequate technical support is to be given to new product development, there must be sufficient return to finance such support over at least the initial years of consumer use while correct usage is being learned. Industry makes its business decisions as best as possible on market-oriented bases, on knowledge of the trends in the foreign and domestic marketplace, and in anticipation of environmental requirements and potential restrictions.

The pesticide chemical R&D process is long and involved. In contrast to many chemicals which move rapidly from initial development to use in products, it is often four to five years after development and registration before the new pesticide chemical will show valid signs of real profitability. Thus, decisions are often made on the basis of limited knowledge of the true potential of the new pesticide and the effort required in its development and marketing. When faced with the decisions regarding the commitment of large R&D expenditures to develop a new pesticide, management must look to the anticipated profitability of the market for the compound, and compare it with the potential return on investment for the development of other chemical products.

The pesticide industry has developed under the constraints and benefits of federal regulation for over 25 years. The possible impact of new pesticide regulations on the innovative activity of pesticide manufacturers, particularly research and development, could be serious for manufacturers, agriculture and the public. Restrictions on use, threat of suspension or cancellation, increases in data requirements, timing, and costs of the registration process could lead to a decrease in innovative activity in the pesticide industry. Such actions could decrease profitability and increase the cost of innovation within the pesticide industry, create a management climate leading to the reallocation of resources and commitments from pesticides to other research pursuits, and increase the risks associated with innovative research. Decreases in innovative activity will ultimately affect the type and quantity of new pesticide products entering the market, alter pesticide production and use patterns, and could result in increased cost of agricultural production. Countering these effects are the potential improvements in human safety and environmental quality, and the development of new pest control techniques brought about in response to new regulatory actions.

The probable effects of past and current regulatory action on innovative research and development activity in the pesticide industry is the subject of this report.

B. PROGRAM OBJECTIVES

The principal objectives of this program were to:

(1) Describe and identify trends in key factors that influence innovative activity in the pesticide industry, e.g., characteristics of the industry, research and development staff, approaches, and costs, characteristics of the market, etc.;

(2) Examine the impacts of past federal pesticide legislation and regulations on innovative activity in the pesticide industry; and

(3) Assess the probable impact of current federal pesticide legislation on innovative activity and suggest methods for minimizing adverse impacts.

Emphasis was placed on studying those market or structural factors which were most relevant to innovative (research and development) activities. The work focused on obtaining and examining industry's reaction to past federal regulatory activities and industry's anticipation of how current and proposed federal regulations would impact future research and development activities.

This report reflects the views of the authors and their interpretation of the views expressed by industry. It has not been reviewed or commented upon by other parties interested in pesticides such as environmental groups, the USDA, or the staffs of academic institutions.

C. APPROACH

A brief review of trade, scientific and regulatory literature covering the past ten years was conducted in order to: (1) describe the R&D process in the pesticide industry; (2) identify companies with pesticide research and development activities; (3) obtain valid sources of necessary market and sales information; and (4) obtain published views of the impact of regulations of innovative activity. Pesticide laws and regulations from the Federal Insecticide, Fungicide and Rodenticide Act of 1947 (FIFRA) to the Federal Environmental Pesticide Control Act (FEPCA, or FIFRA amended) were examined and compared. A series of scenarios depicting possible implementation strategies for FEPCA and resultant potential impacts on innovative activities were prepared. Companies with major pesticide research and development activities were identified, and discussions were held with 22 companies representing large and small, established and newly formed segments of the pesticide industry. The discussions involved personnel from management, marketing, financial, research, engineering, regulatory liaison and legal staffs of the industry. The discussions focused on: (1) the principal impacts of past regulations on R&D activities; (2) the anticipated implementation of FEPCA and its potential effects on R&D activities; (3) recommendations for mitigating any adverse effects of FEPCA implementation; and (4) data which demonstrated trends in research and development and impacts of regulations. Our reception at industry was excellent; discussions were open and frank. This was made possible in part by industry's desire to provide some "feedback" to EPA through an independent party and by our agreement not to directly associate specific comments, data or information with any particular company or product. Even with this agreement, some companies were reluctant to provide us factual data on costs, profits, markets, research timing or staffing. In our discussions and data collection at industry, we attempted not to duplicate the forthcoming National Agricultural Chemical Association (NACA) survey (an update of the 1970 survey) nor to duplicate information that was prepared by industry in response to publication of proposed regulations. We also discussed the implementation of the current regulations with NACA staff and EPA registration staff. The notes, comments and data obtained in these discussions were examined, analyzed and integrated into this report.

D. REPORT ORGANIZATION

Section III presents a brief background description of the pesticide industry, focusing on research and development activities. The pesticide research process is described, and trends in R&D staffing, expenditures, time frame, and outputs are presented. Section IV summarizes and compares the major regulatory actions from 1947--FIFRA--to 1972--FEPCA. A discussion of the possible specific impacts of FEPCA and its regulations is next presented, followed by a discussion of more general impacts of the regulations and other factors on R&D activities in industry. Topics may be discussed in more than one of these sections since they may represent trends in industry as well as impacts of both past legislation and FEPCA. Section V presents industry's and ADL's recommendations to minimize the impact of FEPCA on R&D and to encourage innovative research. Finally, the major study conclusions are given.

III. TRENDS IN THE PESTICIDE INDUSTRY AND THE R&D PROCESS

A. THE PESTICIDE INDUSTRY

In 1971 the U. S. Tariff Commission reported that 87 companies produced basic pesticides. Only a few can be considered "pesticide companies," i.e., companies which concentrate almost all of their effort on pesticides. Most are multi-product companies which produce a variety of chemicals. Some concentrate heavily on agricultural products (40-100% total business) while others rely on agricultural products for less than 15% of their business. Most of the companies which contribute significantly to pesticide R&D are in this latter category.

Figure 1 shows the channels of development, production, formulation, and distribution of pesticides. In most cases, two or more functions are assumed by the same company. For example, a company may develop and formulate its own product, relying on some basic chemical producer to manufacture the active chemical. In other cases, a developer will license a chemical to a company which will both produce and formulate the product. Other combinations are common. In the recent past there has been a small trend towards vertical integration, i.e., a company carrying a product from development to retailer. This circumvention of distributor is a relatively new occurrence and has not been notably successful.

Companies can enter the pesticide business by assuming any of the roles mentioned above, although not necessarily with ease. To enter the manufacturing or R&D phase, companies can:

1. License potential chemicals or purchase the patent rights of pesticidal chemicals developed by other companies.

2. Manufacture non-proprietary chemicals if a competitive edge can be gained in marketing or by an improved manufacturing process.

3. Purchase small companies already involved in pesticide development or manufacturing or both.

4. "Start from scratch" with the development and manufacturing of proprietary compounds.

5. Expand and diversity existing, related activities to include pesticide development and manufacturing.

Companies generally either make a large initial investment with the laboratory equipment, farm facilities and highly qualified professionals representing several disciplines; or make a small initial investment, giving a few professionals some lab space and allowing them to "see if they can come up with something." Many of the firms that have conducted

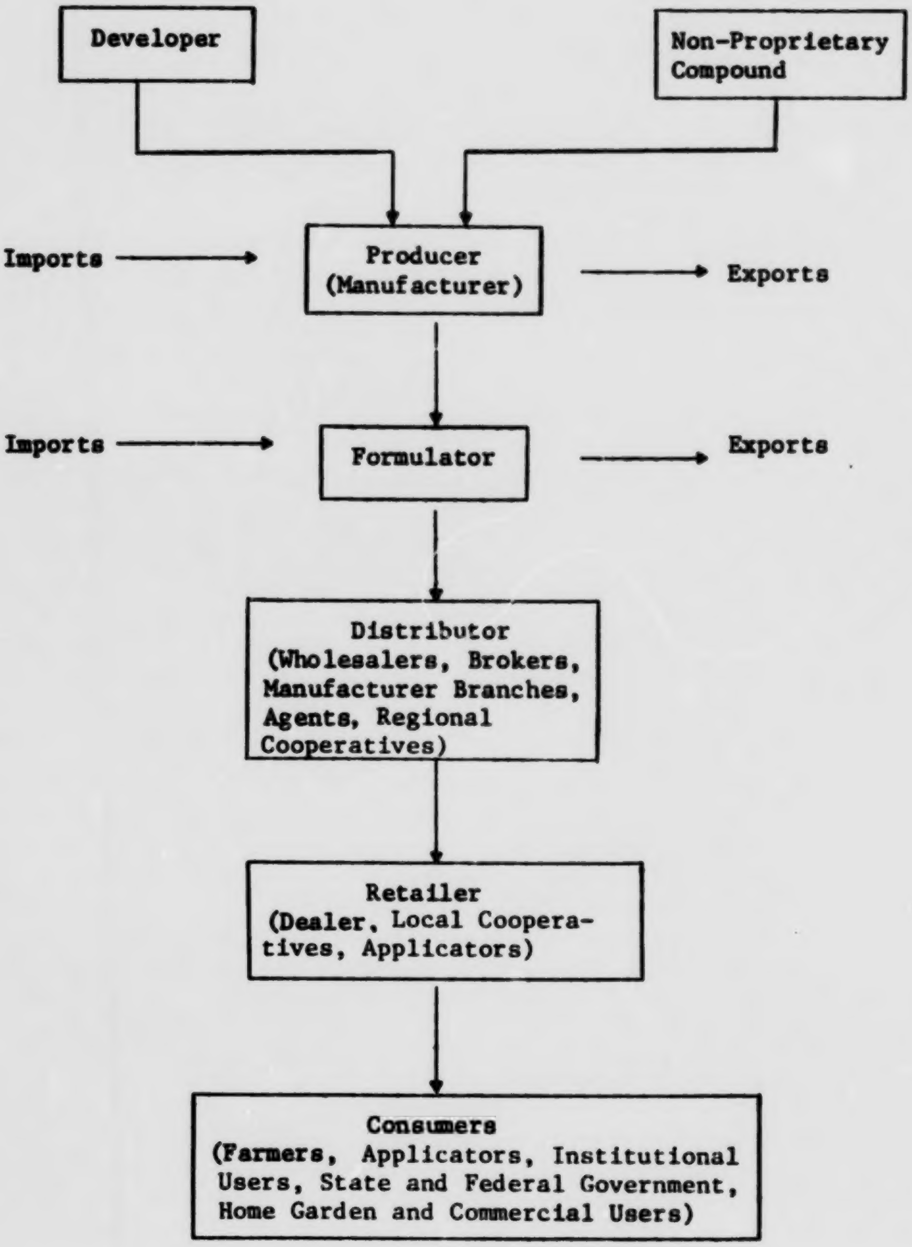
Developer
Non-Proprietary Compound
Imports
Producer (Manufacturer)
Exports
Imports
Formulator
Exports
Distributor (Wholesalers, Brokers, Manufacturer Branches, Agents, Regional Cooperatives)
Retailer (Dealer, Local Cooperatives, Applicators)
Consumers (Farmers, Applicators, Institutional Users, State and Federal Government, Home Garden and Commercial Users)

FIGURE 1. CHANNELS OF PESTICIDE DEVELOPMENT AND SALE

research and development for 10 to 20 or more years started by this latter method, the "Edisonian" approach, while more recent entrants have either made a large investment of manpower, etc., or have purchased another company. Most companies involved in pesticide R&D indicate that a large initial investment is necessary in today's competitive market. The recommended minimum for entering the pesticide business (starting from scratch) is:

- $7 million to develop the first pesticide and a total of $50 million to commercialize the first successful product to the point of obtaining significant return on investment.
- 10 years of "dry time" until a return is seen on the investment. This includes discovery, testing, registration, plant construction, and initial marketing efforts.

The magnitude of this initial effort limits the type and size of organizations which can enter pesticide research and development. In most cases, only larger firms can risk this amount of money with no return on their investment for ten years. One company we contacted referred to pesticide R&D as a "poker game," with only the larger firms able to risk the initial ante. Larger firms also have other product lines which can support the "dry times" both in developing initial compounds and in the continuing development of further compounds. Some of the companies now conducting R&D initially purchased patent rights or licensed pesticidal compounds to provide the continuing income necessary to get over these times.

Currently there are about 30 companies which contribute to innovative research and development in pesticides in the U. S. Most of these are multi-product firms for which pesticides comprise less than 20%, and in some cases less than 1%, of their total sales. About 70% of the companies which contribute to pesticide research and development are large basic chemical companies, including the major oil companies. Large multi-product pharmaceutical companies comprise another 10% of the firms which conduct pesticide research and development. The final 20% is comprised of a wide variety of smaller firms. Pesticide sales in these smaller firms can make up anywhere from 20-100% of total sales.

The multi-product companies have a common basis in their starting points for R&D, both in terms of developing products and initial entry into the business. They all have active synthesis activities which make large numbers of organic compounds available for screening. The major chemical companies screen 5,000-10,000 compounds for pesticide activity per successful product. The compounds may be chosen at random from synthesis activities in other product lines, or they may be synthesized by structural modification of a known class of pesticides. Historically, the empirical method of random screening has been the most widely used approach to pesticide research although all companies now combine this approach with the more directed method for discovery which relies on prediction of biological activity and synthesis of appropriate compounds based on the knowledge of the crop and pest. It appears that the use of the directed synthesis approach, which involves less risk and cost, will continue to increase with the gradual accumulation of fundamental biochemical knowledge.

Since most of the companies which conduct pesticide R&D are multiproduct by nature, it is useful to compare the relative attractiveness of the pesticide product line with other chemical and pharmaceutical activities. Within large firms the various product divisions compete for research money as distributed by management, and there is an ever present possibility that management will decide to rechannel pesticide efforts into other product lines. Some of the factors which contribute to decisions to stay in or to get out of the pesticide business are the following.

Rate of return and profitability--As mentioned earlier, there is an initial "dry time" of up to ten years before a company which has just entered the pesticide R&D area can expect to commercialize a product (unless they have bought an existing pesticide firm or have unusual luck). Once a company has become established in the pesticide area the average time before obtaining the return on investment made for a specific potential product averages about 8 years. Managers in the pesticide divisions of these large firms are often concerned that this time period exceeds the "half-life" of the average decision maker in top management, and that products involving less time for return, e.g., plastics with a four-year development time, might be favored for that reason. Turnover in management seems to be a problem in those large firms which have not yet developed their first successful compound.

For individual products the rate of return and profitability after commercialization of a product varies considerably. Rates of return as low as 25-30% are acceptable to some companies if an $8-10 million market is assured. For a $3-4 million market, a minimum of 40% rate of return is acceptable. Profitability, of course, is also a factor. For some companies a 10% profitability is necessary with a market of $100 million gross sales. Other companies generally expect 25-30% profitability. The percent profitability generally depends on the relation of the total expected sales volume to the minimum sales required to contribute significantly to company profits and to make up for development effort spent on products which never could be marketed successfully. Pesticides, in general, are lower in profit but higher in total sales than other specialty chemical products such as pharmaceuticals.

Companies involved in pesticide R&D have increasingly turned toward higher profitability pesticides, i.e., herbicides, which in most cases are more profitable than insecticides. Some companies are becoming increasingly concerned about delays in getting a product out on a market because the price that consumers are willing to pay and thus the profitability of the product often depends on its newness to the field.

1. Risks in the Development Process

Generally, random screening of compounds in pesticide research yields a success to failure ratio of 1 to 7,000 (the lowest reported in our discussions with industry was 1:5,000, the highest, 1:20,000). Not all failures are eliminated early in the research process. One company stated that: the investment needed to find out whether a pesticide was going to be viable (both from the marketing and registration point of view) comprised about 50 to 60% of the entire cost of development, and that this investment has increased from about 30% in 1968. The timing of the decision on whether a compound is viable varies widely with the company, but for most it involves at least two screening processes. Most companies indicate that the difficulty in making market projections so far in advance (because of the long registration process) compounds the risk involved in a "go-ahead" decision on a pesticide product. Some companies plan to make that decision within the first two years of the development of a pesticide so that they can obtain commitments from raw material suppliers. Therefore, the companies have to anticipate market factors 6-8 years in advance. Thus, the development of pesticides often involves more risks than the development of many other products. The risk presented by investment in product facilities, although large, is no greater than that of other product lines in other industries.

Although the risk and time required for a return on investment would seem to make other product lines more attractive, the fact that there are a large number of multi-product firms involved in pesticide R&D indicates that other factors such as volume, sales and profitability may counteract these negative factors. The risk, and "dry time" seem to become more important, however, if the company is just getting into the business and does not yet have products on the market to support the ongoing research efforts. This is the time when pesticide R&D efforts are especially susceptible to management "cold feet" or lack of "patient money."

The adaptability of the pesticide R&D investment to conversion to other product lines is determined by several factors:

- Manpower--the large numbers of organic chemists and technicians required for synthesis and process development are substitutable. However, the specialized plant pathologists, biochemists, entomogolists, and other crop and pest specialists cannot be transferred to other product lines. This is confirmed by reports of companies "getting out of the business" attempting to help their more specialized staff obtain jobs in other companies which are continuing their pesticide R&D work.

- Facilities--With increasing sophistication in environmental testing and the need to cut down on delays, companies are required to invest in more specialized expensive equipment in the overall pesticide development process. This equipment and screening facilities, such as insect labs and greenhouses, are not substitutable. Farmland for field testing is easily reverted to capital.

- Production--The largest investment in developing a pesticide product line is the capital needed for the plant that will produce the product. This represents an investment of up to $30 million in many cases. This plant may or may not be adaptable for other uses. Some of the equipment may be used for other chemical processes, but there are likely to be particular processes required by the production of the pesticide which necessitates the use of specialized equipment. It is often difficult to find other uses for this specialized, and often expensive, equipment. If it is possible to use the plant for other products, it usually does not yield the most cost effective process for this other production.

- The stage of development of a pesticide line--If a company decides to drop out of the business before it has gone into production of a salable chemical, the transition can be made with a capital loss of about $1-10 million depending on the amount of equipment, tests, manpower acquired, and whether a pilot plant was built for production of the chemical for experimental use.

Companies that have been successful in the pesticide R&D area and have developed a diversity of successful products reported to us that they would go into pesticide R&D area again if presented with the opportunity today.

Companies that have been only moderately successful stated in our discussions they would either decide immediately that the risk was too high or drop out during the long wait for return on their investment. The small investment and Edisonian approach to research is no longer possible today. The initial investment of past years did not involve the facilities and manpower which are necessary today for environmental and safety tests which are part of pesticide development. The increases in the development costs came slowly to companies that were able to use this approach and were supported by pesticide products which were already on the market. New companies however have to make an initial investment which reflects the increased development costs.

The resultant trends are:

1. Multi-product firms already in the pesticide business will continue to be the main contributors to pesticide R&D since they have the income to provide continuous support to the investment requirements of pesticide development.

2. Most of the pesticide R&D will continue to be done by a combination of random screening of compounds synthesized for a variety of efforts and screening of compounds specifically synthesized for pesticidal activity. This latter method will

continue to grow in importance.

3. While a few new companies will enter the pesticide R&D area, there will be a general consolidation of pesticide R&D companies centering around companies that have a well established pesticide product line and can support the continued development of new pesticides.

4. If risk and rate of return stay at present levels, pesticides will continue to compete effectively for R&D dollars within multi-product firms.

2. Trends in Pesticide Products

Herbicides--In the mid-sixties a few new herbicides became spectacular successes as profitable compounds because they were timely in filling the need to increase manpower productivity and yields. As a result many companies placed increased emphasis on herbicidal screening which has led to a rapid increase in the number of herbicides on the market. Many of these products are closely related based on similar chemical structures indicating a rapid synthesis of related compounds by industry based on the initial successful herbicides.

Insecticides--Currently less R&D is being done in the insecticide area than in the herbicide area because of the general lower profitability of insecticides. Research has moved away from chlorinated hydrocarbons because of their persistence and other environmental problems. Many organophosphates came onto the market in the early fifties and they continue to be a focus of research. Carbamates have developed more recently and have begun to assume a significant role in the industry. Much of the innovation in the insecticide area is coming from basic research and a better understanding of the comparative insect and mammalian enzyme systems. The search for insecticidal compounds is directed toward disrupting particular enzyme reactions that became known through this basic research. In a similar way, hormone systems have come into focus for pesticide R&D. For example, as the stages of growth of particular insects are understood, chemical analogs of the hormones which trigger these stages of growth can be synthesized and used to disrupt growth patterns. Juvenile hormones act in this way preventing insects from reaching the reproduction stage.

Juvenile hormones and most pheromones are not viewed by industry as biological controls since they are chemicals, which act in the same way as other chemical controls, i.e., by disrupting the normal chemical reactions of the insect. Those that are considered to be biological controls are general bacteria and viruses. Thus, there are three major categories of insect control methods:

(1) Synthetic organic and inorganic chemicals which act as toxicants to the organism;

(2) Synthetic organic chemicals which are analogs or naturally occurring insect chemicals and which disrupt a particular stage of growth or reproduction; and

(3) Naturally occurring pesticide compounds, e.g., bacteria and viruses, which are selectively toxic to particular insects or other pests.

Generally, there has been a continuing predominance of type (1) compounds since this is the natural outcome of the empirical approach to research, i.e., the screening of a wide variety of compounds. There has been a very slow increase in type (2) compounds but they do not as yet comprise a significant part of the market, nor has their utility as a means of insect control been firmly established. Some companies are finding them to be too specific in nature, i.e., the target pest does not comprise a potentially large enough market to justify the development costs. Bacteria and viruses have received attention from only a smaller number of companies (about five), and some of these are curtailing their efforts in this field. The reasons for this will be discussed later.

Fungicides--High value fruit and vegetable crops, for which high quality is a necessity for sale, are the primary markets for fungicides. The market comprised by the high-value fruits and vegetables is near to being saturated since there is little room to increase usage per acre, and acreage increases in these crops will be minimal in the future. Therefore very little directed research will focus on fungicides, although, as one company we interviewed stated, "if one was found in their regular screening process that could be developed and made cheaply, they would proceed with it."

3. Trends in Minor and Major Use Pesticides

As stated in the discussion on insecticides, some companies find that the compounds which are designed to be specific (narrow as opposed to broad spectrum) are often too specific, that is, the particular pest does not comprise a large enough market to justify the development cost. With increasing emphasis placed on the companies to develop specific pesticides, companies are directing their efforts toward the major markets. Among the larger companies which demand a larger volume of sales, the major markets are comprised by: corn, cotton, soybeans, small grains, rice, alfalfa. (Rice is included as a major market by those companies with foreign as well as domestic markets.) Some of these companies have begun eliminating, early in the screening process, compounds which do not show promise in one of these major markets. Some of the smaller companies (<$500 million net sales) consider citrus fruits, apples and some other fruits to be major markets. The definition of major market depends on the sales volume required to meet development and overhead costs as well as to contribute significantly to company profit. Currently, about half of the products on the market were developed for minor uses, for example, strawberries, cumquats, etc. New products for these markets may only be developed if they constitute additional uses for compounds developed for major markets. Additionally, some of the products currently registered for minor uses may be eliminated if their sales volumes cannot justify the costs of reregistration. The major and minor uses will be discussed in more detail later; here they are mentioned as trends in product development.

4. Trends in Market Factors

Competition and substitutability--In both the herbicide and insecticide market there is much competition between producers. In the herbicide market, for example, Amchem competes with Elanco for the soybean market; both Amiben and Treflan are used for pre-emergence weed control. Shell competes with Elanco in the cotton market and with both Elanco and Amchem for the soybean market. In the insecticide area, competition exists among Shell, Velsicol, Chemagro, American Cynamid, and Hercules, all of which produce products for use on cotton foliage. Chemagro and American Cynamid also supply systematic products for use on cotton.

Most companies state that the existence of one or more products that already occupy a market niche does not stop them from developing compounds for that use. In fact, the companies feel it necessary to develop new—but better--products for the same use even if it involves competing with their own products since they are aware that other companies will be pursuing the same use with new products. Industry predicts that the competition will increase in products which involve major uses (cotton, soybeans, etc.).

Competitive products are never entirely "substitutable" since they involve differing efficacies and environmental and safety factors. However many products are substitutable to the point that they help eliminate the same pest organism. Sometimes a producer which has a commanding share of a particular market will offer several products which can be alternated to avoid build up of a single residue in the soil and to avoid resistance. Farmers may change products on their own to prevent this from happening.

Foreign vs. domestic markets--U. S. producers contribute significantly in the world market with Canada and Latin America being the most important export market. The market in Europe is increasing rapidly. Pesticide exports will continue to grow, but other countries are increasing their pesticide production capacity. Japan, for instance, is becoming a large exporter of pesticides, although it continues to serve as a market for American pesticides.* Several American manufacturers are beginning to become more involved in foreign product ventures, including American Cyanamid in Italy, Hercules in Central America, Velsicol in Mexico, and Rohm and Haas, Dow, Rorer-Amchem and others in Japan.

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*Source: Trask, Harry A., U. S. Pesticide Industry 1967-1972, Arthur D. Little, Inc. Service to Management Report, 1968, p 13.

There has been an increasing tendency for companies based in the U. S. to turn to foreign markets to supplement domestic sales. It is easier to obtain registrations in some other countries, since companies which have only domestic plants generally wait to see whether they obtain registration in the U. S., in order to know when and how large a plant to build.

Government action--Government support programs generally increase pesticide use. When farmers are guaranteed a support price for crops under these programs, they tend to use more pesticides in order to grow them more economically. For example, if government programs are based on acreage controls, farmers tend to utilize more pesticides in order to increase production per acre. If programs are based on production controls, farmers tend to utilize more pesticides in order to minimize the acreage and thus the cost needed to produce their allotted quantities.

AID programs have influenced the amount of herbicides and insecticides exported. As countries increase their food production it is unlikely that they can increase pesticide facilities fast enough to cause a significant decrease in pesticides exported in the AID program. Lately AID programs have promoted increased exports of corn and soybeans to help build up animal industries. These crops are large users of herbicides and therefore an increase in production of these herbicides may be expected.

Military Use--The use of defoliants in South Vietnam significantly increased the production of 2,4,-D and 2,4,5-T, Tordon and organic arsenicals. The end to a significant portion of this demand has resulted in some of the companies, which relied on this production, to consider withdrawal from this market.

Demand--The continued increase in volume of sales despite sharp increases in the prices of many pesticides within the last year indicates a continued increase in demand. Most of this is due to an increase in domestic agricultural production in the last two years. Foreign demand has not risen so sharply. Part of the price increase is due to increased prices of raw materials. Additionally, over the years there has been an increased willingness on the part of the farmer to take extra precautions. As food prices rise, the farmers may be willing to spend additional money on fertilizers, improved varieties of seeds, causing additional expenditures for pesticides to be made to protect these investments. In the past year there has been a shortage of pesticides as a result of petroleum (raw material) shortages, so that farmers have not always been able to meet their requirements.

The demand for herbicides has increased, for instance, because farmers have become more aware of crop losses represented by weeds making use of the large amounts of fertilizers applied for the crop. Increased demand for herbicides also reflects the decreasing supply and resulting higher cost of farm labor. Farmers have traditionally combatted weeds with mechanical or hand labor but now they are willing to spend more for chemicals to do the same jobs.

The elasticity of demand differs for individual pesticides and for pesticides as a whole. The demand for pesticides as a whole is relatively inelastic, that is, price fluctuations in pesticides do not affect the total demand which is controlled more extensively by other factors such as cost effectiveness, value of the crop, the seasonal nature of a particular infestation, and the weather. Among individual major crops, however, the competition among products which eliminate the same pest is high, and the elasticity of demand is high. For instance, if a product patent life runs out and the price is cut by "me-too" firms, it is likely that a particular compound will experience a significant increase in demand. Minor crops, on the other hand, may present a very inelastic demand because of the lack of more than one product to deal with particular pests.

B. THE R&D PROCESS

The discovery and development of a pesticide chemical is divided into the following stages: synthesis and preliminary biological screening, secondary biological evaluation, and small plot field testing; obtaining an experimental use permit; large scale field testing, environmental analysis, and toxicity tests; and full registration. Figure 2 shows the timing of the various stages within the R&D process. The data do not represent the development of any existing compound or the particular process followed by any one company. It is intended to show the relative duration and placement of the various efforts within the R&D process.

1. Synthesis and Screening

This initial stage is designed to identify compounds which show biological activity and could be used to control some pest organism. As described previously, most companies have a dual approach to the synthesis/screening process. On one hand, there is the "shotgun" approach in which compounds from non-pesticide related activities are randomly screened. These compounds can come from other parts of the same company or from other companies through agreements. The chances of discovering pesticidal activity by this shotgun method is low, about 1 in 30,000. Most companies which rely on this method have a large number of compounds which are synthesized for other uses, e.g., pharmaceuticals. Some smaller companies will purchase compounds which are rejected by multi-product companies and screen them for pesticidal activity.

The second approach to synthesis/screening is the "rifle" approach which focuses on functional groups known to have pesticidal activity. Compounds are synthesized by chemists, which number about 5 to 10 persons in many companies. The focus of their synthesis comes from the known functional groups and from modes of action in pest control which are identified by entomologists and plant physiologists on the staff. This approach to synthesis generally yields a much higher percentage of successful products. The more "hungry" a company is for new compounds, i.e.,

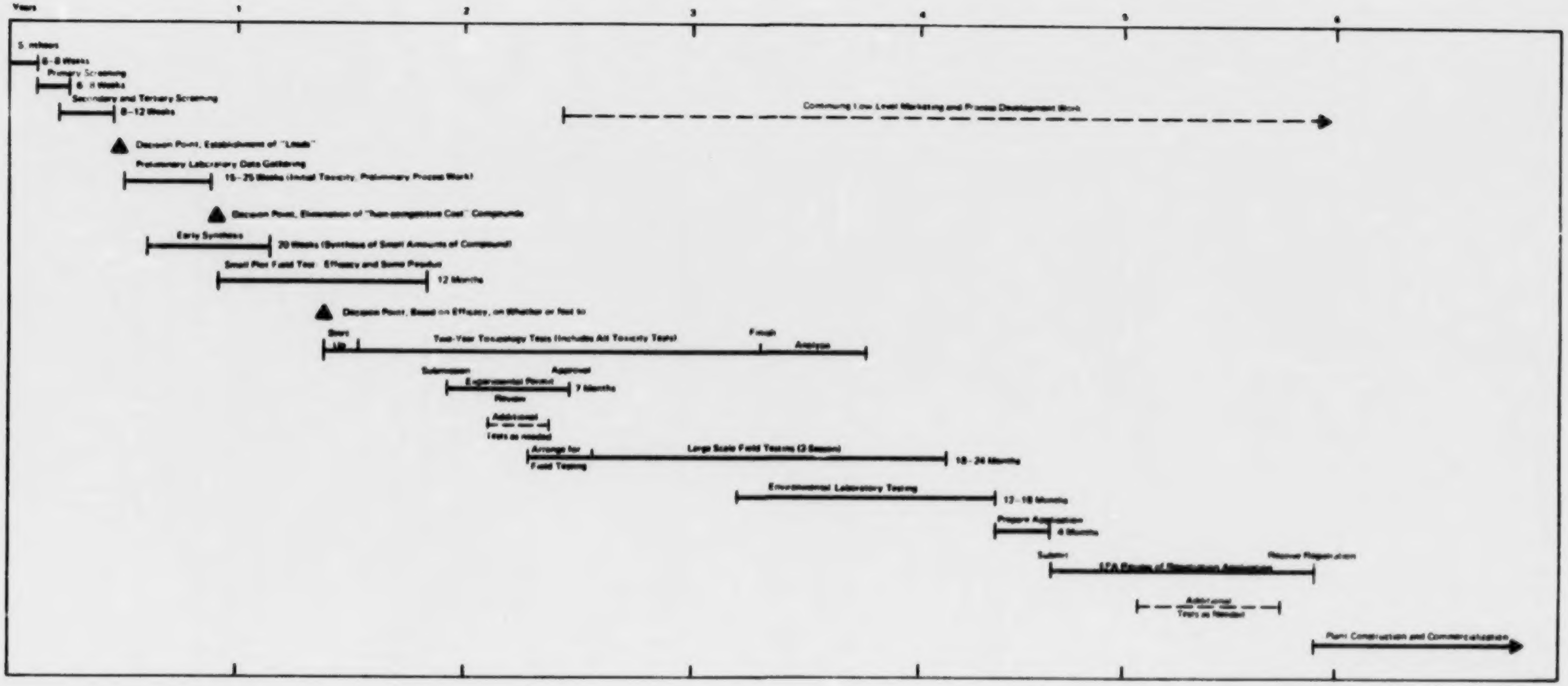

FIGURE 2 REPRESENTATIVE TIMING OF PESTICIDE DISCOVERY AND DEVELOPMENT

the more a company is dependent on new pesticide development for its continuing income, the more emphasis this directed approach is given. In 1970, the NACA study estimated that this directed approach represented about 45% of all screened compounds. Because of the increased cost of R&D and the necessity to have a greater percentage of successes to failures, it is expected that this selective approach to synthesis will become more important. This approach is not likely to result in the development of fundamentally new classes of pesticides.

The primary screening for all types of compounds is a relatively simple operation requiring skill in the interpretation of results. For herbicidal activity for instance, the compounds are applied to a variety of plants which are grown in flats in a greenhouse. These plants include both weeds and crops. Herbicidal activity is present, simply, if the compound selectively inhibits the growth of one or more of the plants. Primary screening usually takes about six to eight weeks. About 7,000 compounds are screened for every successful commercialized product. About 90% of the compounds fall out in this first screening. Two or three biologists supervise this primary screen which is mainly performed by technicians. Although the process is tedious and time-consuming, both technicians and supervisors must be skilled in recognizing subtle evidence of biological activity which characterizes potential commercial successes. According to the NACA survey, about 27% of all compounds screened are screened for all types of pesticidal activities including herbicides, insecticides, fungicides, and others. About 24% are screened only for herbicides, 20% only for insecticides, and 15% only for fungicides. The remainder are screened for other more specialized uses. The interest expressed by many companies in emphasizing herbicide activity has increased since the mid sixties.

Secondary and tertiary screening involves similar activity but with more careful examination involving a greater variety of plants and conditions. This process takes between 8 and 12 weeks and in many companies involves 6 to 8 biologists, entomologists or plant physiologists. It eliminates another 90% of the compounds. Various chemical concentrations are examined at this stage along with types of applications, e.g., direct leaf applications, application to the soil, etc. At this stage the scientists attempt to determine the mode of action involved in any pesticidal activity present. If they believe that possible modifications to the structure of the compound would be more effective in the mode of action, a modified compound is synthesized and screened. About 700 compounds go through this secondary and tertiary screening for every successful product.

At the end of the secondary and tertiary screening there is a review of the products which have survived this stage. This is usually done by a group of people representing various disciplines of pesticide development including representatives from chemistry, biology, toxicology, environment, marketing and process development. Although the compounds under consideration have not been tested in many of these areas, knowledge and experience with similar compounds will aid in the decision-making process. The purpose of this review is to define lead compounds which deserve further investment for laboratory and field testing. At this time synthesis chemists devote some of their efforts to the development of analogs and homologs of the particular compounds. Also at this time patent protection is initiated.

2. Secondary Biological Evaluation

Resynthesis of larger quantities of lead compounds begins after this review period. The purpose of this resynthesis is twofold: to obtain the necessary amounts of compounds for laboratory, toxicological and field testing, and to obtain very preliminary process development data to help determine the projected cost of producing the lead compounds. This synthesis usually goes on for about 20 weeks and involves three or four chemists. At the same time preliminary laboratory work is being done to obtain initial toxicological data. This information will help in the next review of these compounds and will also determine how the compound should be handled in future laboratory and field testing for the safety of the personnel involved. Accordingly these tests include primarily acute oral and dermal toxicity tests. This preliminary toxicity testing takes from 15 to 25 weeks.

At this time another review of the lead compounds is made to assess the information provided in the toxicity and process development work. An important factor at this point is the projected cost of producing the product if they proceed with development to commercialization. The marketing personnel are asked to assess the competitive costs necessary to enter the market at the time of projected commercialization. This is compared to the cost estimates provided by the synthesis and process development personnel based on their preliminary work. If the projected costs of producing the compound is greater than products already on the market or projected to be on the market, the project is dropped. If the projected costs are conducive to further development the toxicity of the compound is assessed to determine whether the toxicity is significantly higher than its projected competitors. High toxicity would make registration, marketing efforts, and consumer acceptance more difficult. About one in 7 compounds pass this decision-making point.

For those compounds that have received a go-ahead decision, process development work is extended to include initial formulation work. At this point about 10-20 pounds of lead compounds are made. Some of this amount is then used for initial small plot field tests. The purpose of this initial field work is to confirm the bioactivity of the product, i.e., its usefulness as a pesticide. Up to now the compound has only been tested in a greenhouse. Although the size of these small plots limits application to only several rows in parallel, this enables observation of the compound under various soil and weather conditions.

At the end of the small plot field testing another review is made by the R&D staff to determine which compounds deserve further investment. This decision is based mainly on the efficacy data acquired in the small plot field tests although environmental factors are considered at this time. (If a compound seems to be environmentally unsound or if toxicity is high, the go-ahead decision is reconsidered.) About one in 10 compounds are chosen for further development at this time--those for which efficacy and costs make the compounds sufficiently attractive to warrant the expense required for registration. At this time the decisions are made as to which compounds need large scale field testing. Those that do will require the large investment for an experimental use permit.

Once this commitment is made to go ahead, with the compound as a potential product, the small plot field tests on the lead compound are extended to include the required efficacy and residue data necessary for the experimental permit. Additionally at this time they start the two-year toxicology tests that are required for full registration. Six months of data from these toxicology tests are necessary for experimental permit application. After compiling the data from the first six months of the toxicology tests, along with the data from efficacy and residue tests, the experimental permit application is prepared and submitted.

3. Experimental Use Permit

On the average, 7 months are required for approval of an experimental permit. This may include resubmission of data required by the first review of the experimental permit application by EPA. Many companies start arranging for the field work while the experimental permit application is being reviewed. Several of the companies, however, have had bad experience as a result of obtaining commitments from participating farmers and institutions, and producing enough compound for the forthcoming field testing on a pilot plant stage, and then finding the approval on their experimental permit has been delayed past the growing season. This results in a loss of money, time, and the potential cooperation of farmers in next year's field program. Most companies submit their application for experimental permit as quickly after the last growing season as possible, i.e., September, so that experimental permit can be approved by January or February. This gives the company time to obtain the necessary materials and cooperation for their large-scale field program.

4. Field Testing and Data Gathering

The duration of the field testing program varies between 18 and 24 months. This includes a required two seasons for testing plus 6 months for data compilation and analysis. The duration required for large-scale field testing is increasing because of the number of regional locations required and the fact that pesticide companies can no longer count on universities for free testing. Industry uses land which they rent or lease from private owners, or land which they have purchased to be used on a continuing basis. Purchasing land is sometimes difficult to justify since each new product demands different regional locations of pests for testing.

The following areas are among those investigated in the large-scale field testing program:

Efficacy--The requirements for full registration require data on the efficacy of the product in solving the pest problem in the various regions in which the product will be used. At times this could involve 50 locations.

Application rates--The large-scale field tests determine the optimum rate of application as well as the optimum method, e.g., aerial spraying, soil application, etc. This information will be used later in formulation studies.

Crop residue--The determination of residue and metabolites in the crop are done in the laboratory but the crops must be harvested at the various locations of the large-scale field tests. Samples of the crops are often frozen at the time of harvest and sent to nearby laboratories for analysis.

Crop rotation--The uptake of the compound and its breakdown products by successive crops in rotation is tested in the second season of the field testing program.

Pathways and levels of ecological penetration--Information on runoff, dispersion of the compound from aerial spraying, entrance into surficial and groundwater systems are assessed for both the compound and its breakdown products. This information is related to environmental laboratory work which is going on in parallel with the field program.

The laboratory environmental effort includes analysis of data and samples from the field program. Additionally such studies as bioconcentration investigations in aqueous systems are done at this time, using indicator organisms such as trout or quail, depending on the particular pathway of ecological penetration which is indicated in the field program. This environmental laboratory work usually begins immediately after the first season of field testing and continues on approximately 8 or 9 months after the end of the field testing program. The total duration for these laboratory environmental studies is about 18 months.

The two-year toxicity tests which were begun prior to the application for experimental permit are generally completed about half way through the field testing program. These toxicity tests include oral LD_{50} and subacute toxicity feeding tests as a minimum, but generally also require reproduction studies, teratogenicity studies, metabolism studies, mutagenicity studies, and other toxicological tests. These tests often require from one to two years. Human hazard evaluation includes eye irritation, dermal irritation and tests for inhalation. The entire duration of these toxicity tests is about 2 1/2 years, including 6 months required for analysis of the data.

5. Registration

The information compiled from the toxicity tests, field program, and the laboratory environmental work is compiled in an application for full registration. Upon receipt of the application EPA reviews the information and compiles all questions from individual reviewers. These are then sent back to the applicant as additional data which are required. Sometimes this requires additional testing, other times it requires merely additional supportive data which was not included in the original application. Upon receipt of the additional information, EPA then reviews the entire application and makes its determination. The average duration of this review process is 15 months.

6. Process Development and Marketing

While the toxicity and environmental testing are being performed, continuous low level efforts are also being expended on marketing and process development including formulation. Once full registration is obtained these efforts increase. It is usually two years from the date of registration to commercialization, if the plant construction has begun before registration. Because this represents such a large expenditure (as much as 20-30 million dollars), many companies wait until they receive reasonable assurance on registration before they start plant construction. If they wait until after full registration to begin plant construction it is usually four years before the product can successfully penetrate the market.

C. TRENDS IN R&D ACTIVITIES

1. Costs

The average estimated cost per compound for discovery and development is $7.6 million including the costs of compounds which were not commercialized. The average cost of the development of the individual compound is $1.8 million. These costs are estimated by industry considering current registration requirements and other research and development costs and represent a hypothetical compound presently being developed. The NACA study reported in 1970 that the cost of discovery and development of a pesticide was approximately 5.5 million dollars and indicated a wide range of costs were reported among the companies participating. The companies participating in our study also indicated a wide range of costs, as shown in Table 1. The cost for similar inventions and developments is perhaps best represented by the cost to develop a new pharmaceutical product, i.e., a specific new drug. In the past few years this cost is estimated to be approximately $6-8 million.

The reasons for the increases in cost vary considerably with individual companies but generally include the increase costs of registration requirements. Registration requirements account for about 20% to 30% of the entire pesticide budget in most companies. The rest is spent on plant pollution controls, marketing and process development. Plant

TABLE 1

ESTIMATED COST OF DISCOVERY AND DEVELOPMENT OF A PESTICIDE

Total R&D Cost Per Successful Compound (Including Rejected Compounds)

RANGE	ESTIMATED AVERAGE
$12,000,000 - $4,000,000 - 1974	$7,400,000 - 1974**
	5,500,000 - 1970*
	6,000,000 - 1969*
	3,400,000 - 1967*

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*NACA survey.

**From 22 companies participating in this survey.

construction accounts for the largest part of the budget, about $20-30 million per product as mentioned earlier.

The overall costs of the entire pesticide development have increased. Some of the factors include:

(1) the growing sophistication of the pesticide industry,

(2) the increased competition among products, and

(3) the increased costs of materials and labor.

The various stages of pesticide and development process have not all increased in cost to the same degree. The areas of R&D which are felt to account for the largest increases are:

(1) Field Testing

Field testing accounts for about 30% of the total cost required to bring an individual compound from synthesis to registration. Recent increases are due in part to the increases in number of regional crop areas needed to fulfill registration test requirements. Some companies report 50 to 100 or more different field tests are required in different parts of the country for major crops. Combining this with the number of tests required at each site (about 5) can lead up to 500 tests being done at the same time for each compound undergoing field testing.

(2) Maintenance of Existing Products

The NACA study in 1970 reported 25% of the R&D budget was being spent on the defense of existing products (for reregistration and for additional uses of the product) compared to 13.4% in 1967. Most companies today report 30%. The increase from 1967 to 1970 was probably due to the reregistration of all compounds according to the finite residue requirements. A wide range of figures was obtained for the percentage of R&D budget spent on reregistration. This percentage may depend in part on how "hungry" a company is for new products, i.e., how long ago the company came out with its last product. If no new products have been developed lately, more effort is spent on the search for new products. If the company has recently been successful in developing a product, more effort will be spent on developing new uses for it.

(3) Personnel and Equipment Costs

Innovative activity has changed over the years because of increased knowledge of structure versus biological activity and the mechanism of action of pesticides. This has led to a need for more educated manpower and more sophisticated equipment. Electronic equipment such as high resolution mass spectrometers and sophisticated data retrieval systems have become important to innovative activity. Additionally, the educational and skill requirements of the scientists involved in R&D are increasing as the knowledge of the mechanism of the biological activity of pesticides becomes more of a factor in discovering a successful compound (specific manpower trends will be discussed in the following section). These increases in expenditures for equipment and manpower are resulting in a higher cost per man year for the R&D process. The data from the NACA survey yields a figure of $65,000 per man year in 1970 as opposed to $47,400 per man year in 1967. The current estimated cost per man year obtained from industry in our study is somewhat lower, about $55,000.

Some information was gathered in this study on the costs to develop existing products. Table 2 shows average costs to develop compounds which were registered in the late 50's as compared to compounds registered in the late 60's. The costs cannot be directly compared to estimated costs discussed above because these costs of existing compounds reflect the requirements of the years preceding the date of registration rather than anticipated costs at that date.

The figures show that one million or less was spent per successful compound in the late 50's and that the costs average as low as $.2 million in 1956 up to and including the first registration. In the late 60's about $1.5 million was spent per successful compound, until 1969 when the cost jumped to $3.2 million, reflecting to some extent the finite residue requirements.

Some of the expenditures per year for various areas of pesticide research provided by one specific company are shown in Table 3. Although the amount of yearly expenditures on insecticides and herbicides vary considerably among industry, some of the other areas of expenditures shown in this table may be more representative. These include the amount spent on basic research done per year in the herbicide and insecticide area, $20,000 and $30,000 respectively. This amount may reflect a general industry policy to study biological mechanisms only as they relate to specific lead compounds, or potential chemical analogs of these compounds. Very little is done in most companies on basic research which would lead to isolated naturally occurring compounds or other innovative methods of control. Most companies questioned preferred that this basic research be done in government or universities.

The amount of R&D as a percentage of sales is often given as an indication of industries' commitment to research. Table 4 shows the annual research expenditure per company in dollars and as a percent of total sales. Pesticide R&D was found to double in dollars from 1965 to 1974 while remaining about the same as a percent of sales. The general impression gained from industry is that this percentage will continue to hold steady for industry in general, although it will vary considerably between companies depending on how "hungry" a company is for new products or committed to the field. By comparison, the pharmaceutical industry devotes about 10% of its sales to R&D efforts, the heavy chemical industry devotes about 2-4%.

TABLE 2

COST OF DEVELOPING COMPOUNDS WHICH HAVE BEEN REGISTERED*

1956	1958	1959	1965	1966	1967	1969
$ 0.2 m	0.3 m	1.0 m	1.5 m	1.5 m	1.6 m	3.2 m

*Data from 22 companies in this survey.

TABLE 3

ESTIMATES FOR PORTIONS OF R&D BUDGET BASED ON ACTUAL COMPANY DATA FOR 1974

	Per Year
Herbicide Basic Biochemical Studies	$ 20,000
Insecticide Basic Biochemical Studies	30,000
Fungicide Product Research	10,000
Herbicide Product Research	200,000
Insecticide Product Research	70,000
Environmental Studies for Above Product Research	460,000
Formulations	290,000
Pollution Control for Production Plant	530,000

TABLE 4

ANNUAL PESTICIDE RESEARCH EXPENDITURES PER COMPANY

	Average	High	Low
1965	$1,363,000	$1,902,000	$250,000
1974	$3,212,000	$6,000,000	$1,000,000

As Percentage of Sales

	Average	High	Low
1965	5.4%	10%	4%
1974	5.9%	8%	3.25%

Source: this study

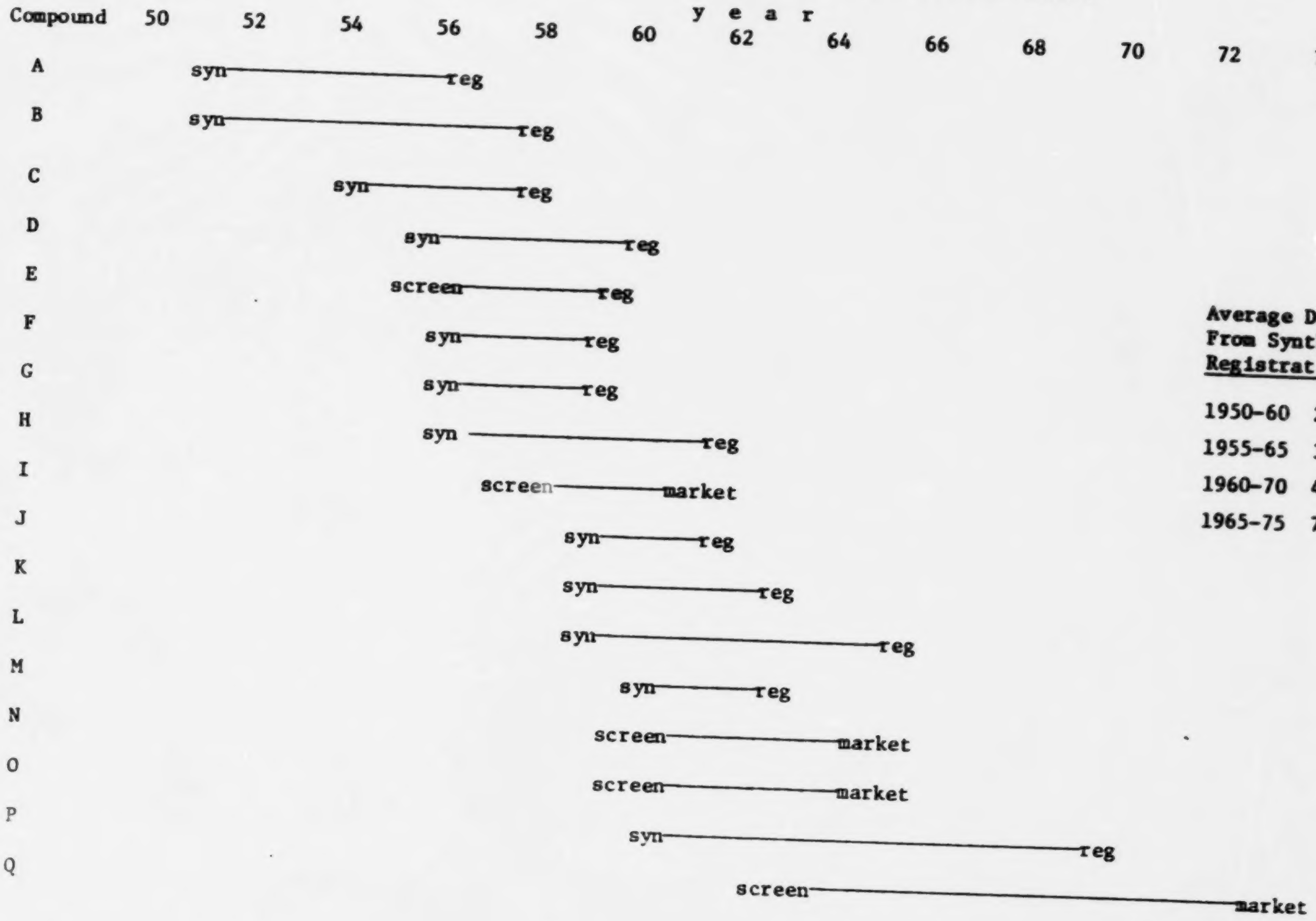
2. Timing

The timing of the R&D process has changed in three general ways: (1) the duration of the R&D process has lengthened, (2) individual areas of effort within the R&D process have increased in time and (3) there has been a re-ordering of the timing of various effects within the process. Figure 3 shows the duration of the R&D development process for representative actual products developed by industry in the 1950's and 1960's. Some of these indicate the duration of effort between synthesis and registration, while others indicate the duration of effort between screening and marketing. The averages (considering only those durations from synthesis to registration) for the yearly intervals between the 1950's and the present show an increase in the duration of the R&D process. Between the years 1950 and 1960 the average length of time needed for development of a pesticide (including registration) was 2.75 years. Between the years 1955 and 1965 this increased only slightly to an average of 3.0 years. A more significant increase is found between the years of 1960 and 1970 when the average duration for the development process was 4.6 years, increasing to 7.0 years between the years 1965 to 1975. The cause of the overall increase in timing can be seen in the increased time needed for specific efforts within the R&D process. In the late 1950's it took approximately 1-4 months to do both the metabolism and the toxicology tests. Now these are part of a 2 1/2 year testing program. The timing required for field testing has increased since it is done now in two stages, one in preparation for the experimental permit and the other in preparation for full registration. The combined efforts for field testing often consumes about 2-3 years of development time. After all the field testing and other testing is done, the time required for registration is also significant. Table 5 shows the average time spent between submission of the application for full registration and the final decision by EPA. This time includes the submission of any additional information required. The time required for registration has increased by a factor of 4 from the late 1950's to the early 1970's. This has been a steady increase with the largest rise occurring from the early 60's to the late 60's.

The shift in timing of individual efforts within the R&D process has generally occurred as a trend towards earlier compilation of data on a wider variety of subjects. This enables early decision-making to be supported by the largest amount of data possible. Like field testing, some of the efforts are divided into two stages: one to give an early indication to include in decision-making, and two to support the application for registration of a candidate compound. Toxicology, for instance, involves three stages of testing: early decision-making, application for experimental permit and application for full registration. This division of effort decreases the efficiency of the R&D effort and adds to the overall time involved.

Figure 4 represents the duration of development of "hypothetical" compounds or estimated R&D timing for "hypothetical" compounds provided to us during discussions with industry. (This differs from Figure 3

FIGURE 3. DURATION OF THE R&D DEVELOPMENT PROCESS FOR REPRESENTATIVE PRODUCTS DEVELOPED IN THE 1950's AND 1960's



Average Duration From Synthesis to Registration	
1950-60	2.75
1955-65	3.0
1960-70	4.6
1965-75	7.0

FIGURE 3 (Continued)

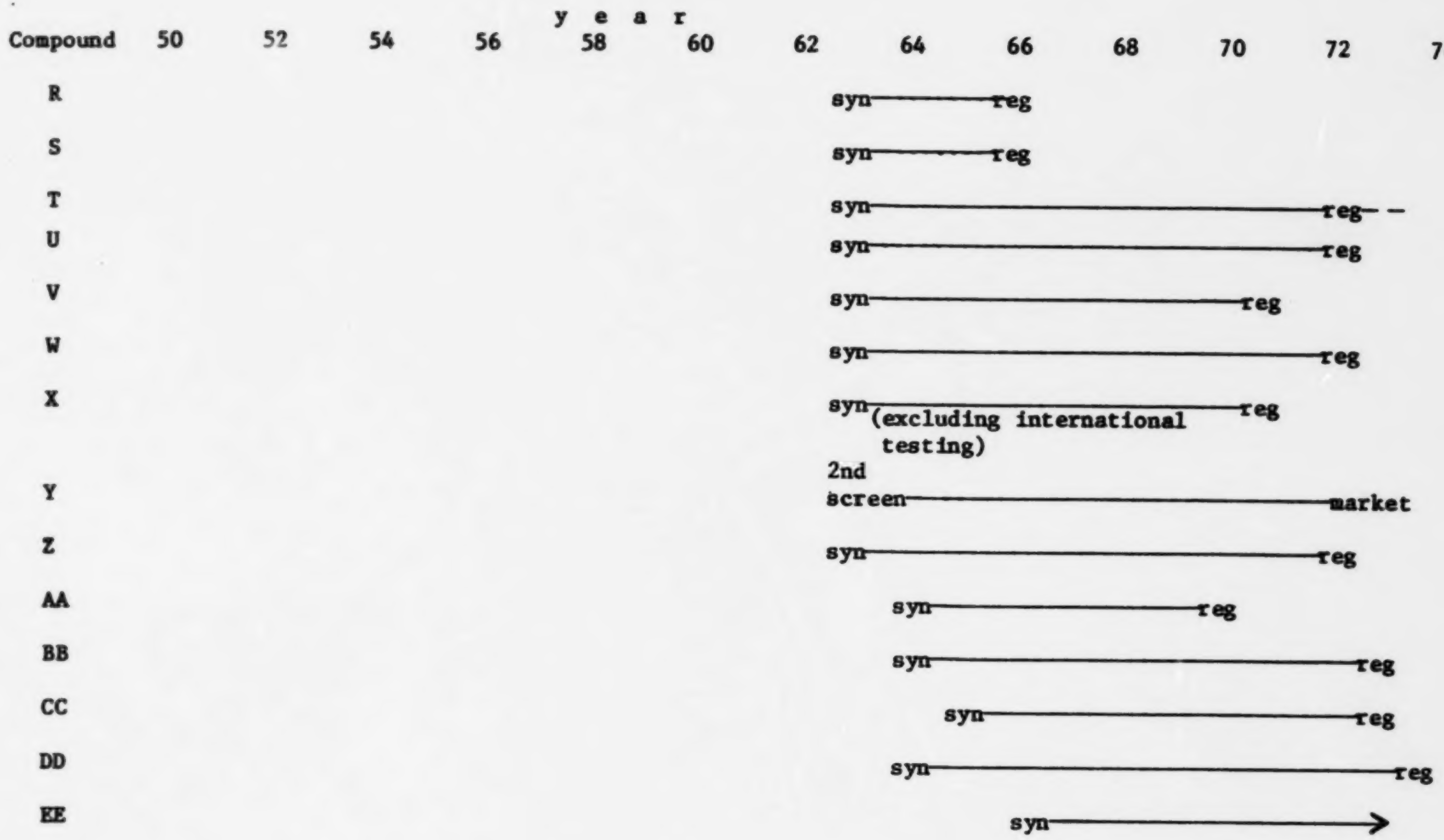
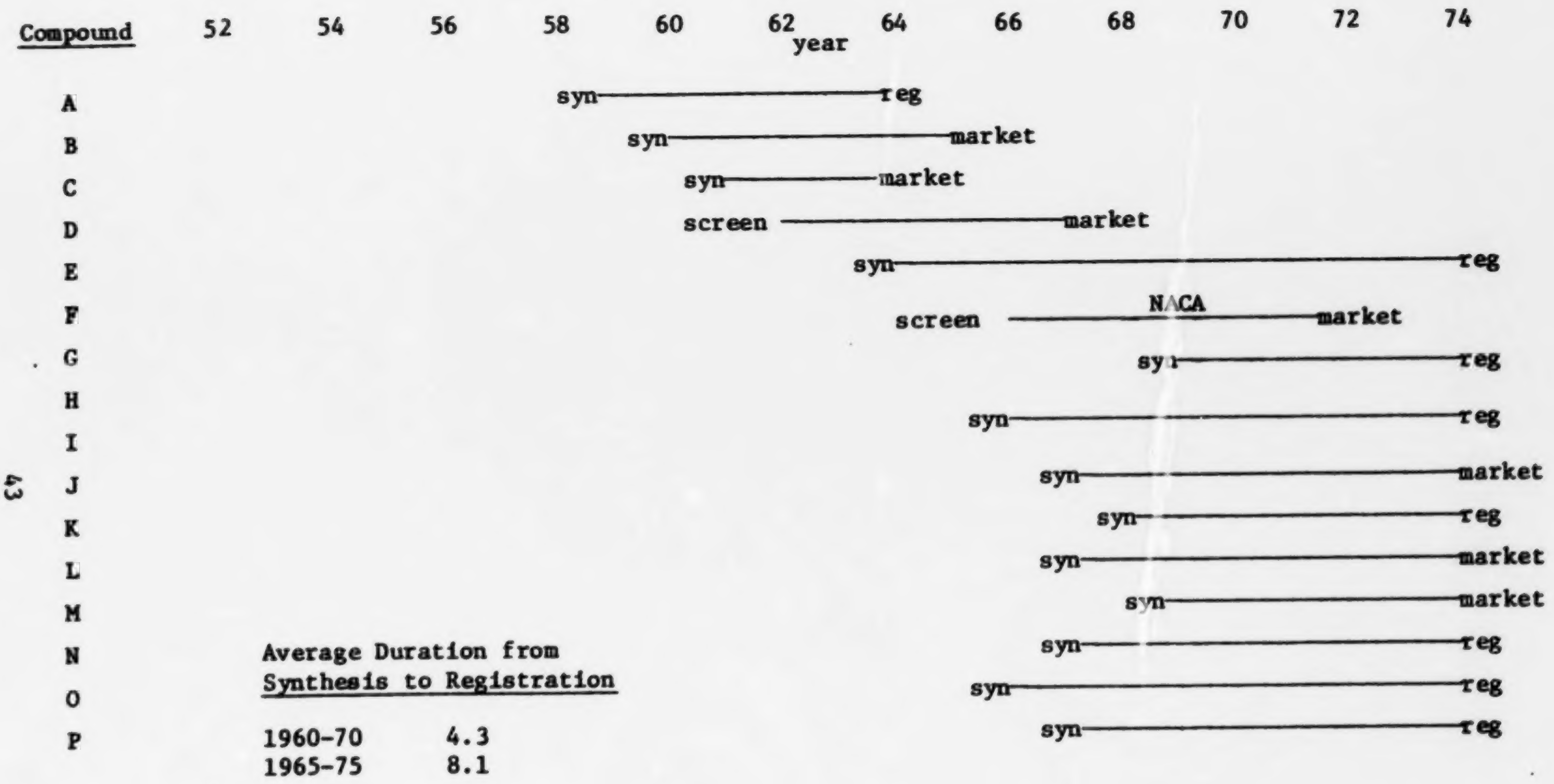


FIGURE 4. ESTIMATES OF DURATION OF DEVELOPMENT FOR HYPOTHETICAL COMPOUNDS



Average Duration from Synthesis to Registration	
1960-70	4.3
1965-75	8.1

TABLE 5

AVERAGE DURATION OF REGISTRATION REVIEW INCLUDING SUBMISSION OF ANY ADDITIONAL INFORMATION REQUIRED

	(Months)
1955-1960	3.5
1960-1965	5
1965-1970	10.8
1970-1975	14.8

TABLE 6

NUMBER OF R&D PERSONNEL IN TYPICAL COMPANIES

	High	Low	Average
1960	100	6	38.8
1965	95	10	54.0
1970	75	18	50.5
1974	188	32	78.5

Source: This study

which represents actual historic data.) Industry estimated that the time required for discovery and development between 1965 and 1975 was 8.1 years, or about one year more than the time needed for those products registered in the early 70's. This additional time reflects current and anticipated development requirements for a hypothetical compound in the process of development today.

3. Manpower

Table 6 shows the average number of professional persons working in representative pesticide companies in 1974, including professionals and technicians and non-technical persons. This average, 78 persons, indicates that the number of professional personnel in the pesticide R&D area has increased significantly since 1970. Generally professionals comprise about 50-60% of the R&D staff with the rest non-technical hourly labor and laboratory technicians. Much of the hourly labor as well as a significant portion of the professional labor is occupied by field testing which, in total, accounts for about 20-25% of the manpower.

The most prevalent trends in manpower seems to be the reshuffling of personnel according to the changing priorities in each company. Some companies have transferred individual scientists, e.g., transferring synthesis chemists to defense of existing products, while others have changed the direction of whole groups, e.g., changing the focus of the biochemical area to help answer the questions posed by the PR 70-15 regulations. The environmental regulatory work on new products and the overall defense of existing products have absorbed most of the shifts in staffing, with the areas suffering the most being new product development, i.e., synthesis and screening. In testing areas that demand personnel beyond the existing capacity of a company, the work is done on a contract basis rather than by hiring additional personnel. Toxicology is one example of a testing area which is often done by contract.

No significant changes in the types or numbers of staff were reported by industry in our study, although a significant increase in more highly educated scientists, especially scientists with Ph.D.'s, was reported for 1970 in the NACA study. Several companies mentioned that they were trying to keep costs down by hiring less experienced persons just graduating from school, or by not hiring highly specialized Ph.D. scientists.

The cost of R&D scientific manpower in the pesticide industry is estimated to be about $50,000 per man year. This is comparable to scientific manpower costs in many other industries, but slightly higher than that estimated for the pharmaceutical industry of $40,000 per man year.

D. DECISION MAKING IN PESTICIDE R&D

Because of increases in time and cost, the decision as to which compounds to develop becomes more important as companies seek to increase their ratios of successes to failures. The decision making comes earlier in product development, and more frequently. This decision making is supported by more efficacy, cost, and safety data, since the increase of risk has led management to require more confirming data both in technical areas and in market areas in order to decide to go ahead with a particular compound.

The relative weights assigned to the decision making factors shape the characteristics of the pesticides that result from the development process by selective screening according to those characteristics. The companies contacted in this study rated the following factors in order of importance in their decision making:

1. Efficacy

The performance of a compound in solving a particular pest problem better than other compounds currently in the market is given highest priority in decisions concerning research and development of compounds. Most compounds are dropped on the basis of (1) selectivity, toxicity, and phytotoxicity, (2) inability to eliminate a greater fraction of the pest problem in equal or less time than current products on the market, (3) instability of the compound in shipment or in the field leading to lack of reliability of effectiveness, (4) ineffectiveness of the compound in the required range of soil and weather conditions.

2. Cost

If a company foresees that the proposed cost of producing a compound is significantly higher than competitive products on the market, this compound will be dropped. The process development work which helps determine the cost of the compound is being done earlier in the development process to assist in this decision. This also puts an added burden on marketing personnel who must assess price fluctuations further in advance.

3. Volume of Market

As discussed previously in regard to major and minor markets, the volume of market needed to develop a potential product varies with the amount spent on the R&D process by individual companies. Some require a $10 million market while others require $500,000 as their minimum market for deciding to go ahead with a potential product. Profitability, of course, is included in the assessment of the volume needed for the return on a product investment. The profitability however does not vary to the same degree as volume, i.e., it cannot compensate for lack of volume in obtaining the needed return on the product investment.

Product development costs for minor uses are usually the same as for major uses since the same development and registration requirements apply to both. In deciding which compounds to develop, some companies eliminate any compound which can only be used on a minor market. Many companies state that the IR-4 programs to develop minor use products needed in individual states has not been adequate in compensating for much of the product development costs. Thus reluctance to develop pesticides for minor crops because of high development costs are a growing concern to some growers' associations and states. One state asked a company we contacted to stockpile a specific compound needed to control a mosquito that had a potential in spreading disease. Because the costs of product development and the sporadic nature of the need for the product and thus the unreliable return on the investment, the company decided that it was too expensive to develop and stockpile the product and it could not meet the state's request. Some companies indicated that they develop a minor use product only if one of the following conditions are met: (1) If it had already been registered for a major use; (2) if it can be used for public relation purposes, i.e., for keeping good will among the consumers who will use other products produced by the company; and (3) if the minor use product is particularly easy to produce.

4. Environmental and Safety Factors

Some companies say that environmental factors have moved back in the decision-making process to become factors in the earlier decision point. The environmental considerations include requirements that the product have a reasonably rapid breakdown in soil and that it not enter the food chain. Others say that if the product is highly toxic they will hesitate to proceed with the development of the compound. Most of these considerations are based on an increase in environmental awareness on the part of both industry and the consumer. Most companies do not feel that safer compounds have an easier time in registration because the same data and testing is required for all compounds. There is a fear, however, that given two equally effective compounds, preference in registration may ultimately occur because of safety or environmental concerns. Any perceived difficulty in registration is carefully considered but in itself will not prevent the development of the compound. Some companies seem to fear the possibility of legal suits based on environmental and safety factors brought by consumers more than any additional registration requirements or possible restrictive use under the law. Several companies in fact said that self-regulation on the basis of this anticipation of consumer legal action would work equally as well as the present law.

In summary, the decision on which compounds to develop is becoming more important as companies try and improve their success to failure ratio. Efficacy and cost are the most important. More compounds get put "on the shelf" for failing in these areas than any others. Anticipated volume of sales is next in importance with decisions favoring major use markets. Toxicological hazards will slow down product "go ahead decisions" primarily because of consumer acceptance of any anticipated extra registration requirements are considered but in themselves do not prevent the development of a compound.

E. TRENDS IN PRODUCT DEVELOPMENT AND INNOVATION

Table 7 shows the average number of new compounds developed and the average number of registrations obtained for representative companies contacted in this study. Between the years of 1960 and 1965 an average of 5.6 compounds were developed per company. Between the years 1965 to 1970 an average of 2.6 compounds were developed per company. The sharp decline in this average may be due in part to a decrease in activity during the years following the issuance of the finite residue requirement during which time industry spent much of its time testing and reregistering its existing products. This decline, however, may also be due to four other factors: 1) fewer compounds are in the process of development due to caution on the part of decision makers in regard to higher costs for the product development process; 2) minor use markets are not receiving attention; 3) a general decrease in the productivity of the R&D process is occurring as a result of the necessity to place effort in the defense of new and existing products, 4) simple, easily developed compounds have already been discovered.

The trend indicated in the number of registrations obtained per company (also shown in Table 7) indicated that companies are continuing to obtain registrations for new uses and new formulation for existing products at the same rate. Between the years 1960 to 1965 an average of 90 registrations were obtained compared to 71 in late 1960's and 75 between the years 1970 and 1974. These registrations include additional uses for existing products, new products, new compound registrations, formulation registrations, and others.

1. Decreases in Particular Types of Compounds

Several companies mentioned that they had gotten out of the insecticide R&D area because of several reasons which will be simplified here for the sake of brevity. Companies have had less success in developing insecticides because new functional groups possessing insecticidal activity have been generally exhausted in the search for new compounds. Additionally, the market for insecticides has been around a longer time and is saturated with inexpensive, non-proprietary compounds which make the cost of producing insecticides a very important factor and one which tends to eliminate compounds early in the development process. Herbicides seem to represent a larger market where higher profits can be expected as extensively. Those companies that have been successful in developing insecticides, however, are staying in that area. Only companies that were only marginally successful in insecticide areas have been affected by this trend. Fungicides have also been eliminated from the screening done by many companies. This is mainly because most fungicides represent minor markets. Additionally, they are generally more specific than either insecticides or herbicides and thus cannot be extended to the same number

TABLE 7

NUMBER OF NEW COMPOUNDS REGISTERED PER COMPANY

1960 - 1965	1965 - 1970	1970 - 1974 (estimated--not enough data available)
5.6	2.6	2.0
Range 1 to 19	Range 0 to 6	Range 1 to 4

TOTAL OF REGISTRATIONS PER COMPANY INCLUDING NEW USES, FORMULATIONS, ETC.

1960 - 1965	1965 - 1970	1970 - 1974
90	71	75

Source: This study

of additional uses. Industry is also avoiding areas that can easily be anticipated to represent large registration requirements that are not compensated by large volume markets. For instance, the rapid distribution of aquatic herbicides into the ecosystem and the extensive environmental testing needed for registration, are making some companies avoid this low volume market.

2. On-the-Shelf Compounds

There is a general feeling among those outside of the industry that there may be compounds on the shelf which companies are holding back until registration requirements become stabilized or less expensive. This was not found to be true. Any compounds on the shelf are there because they were eliminated in the decision-making process as either too costly, non-effective, or unsafe. Furthermore, all decisions on developing a compound are based on a precise timing for entrance into the market. Compounds cannot be held back if a company expects to gain its projected return on development since a competition may beat them to the market with a better product.

3. Biological Controls

In regard to decision-making factors discussed above--efficacy, cost, market volume and safety--industry in general does not consider biological controls worth pursuing.

Only one company, Zoecon Corporation, was found to be devoting their major effort to the development of hormonal control methods. Other companies in the pesticide industry are watching this firm closely to see if such biological controls can be a successful venture if pursued vigorously. The degree of involvement of other companies in the biological control field varies with the type of compound considered, i.e., whether it is a synthesized analog of a natural occurring substance, e.g., juvenile hormones or whether it is the naturally occurring substance itself, e.g., bacteria and viruses. In general industry regards biological controls as being the latter. About 20% of the companies contacted in this study are maintaining some level of effort in the "synthesized biological" controls. Most of the work is being done in juvenile hormones and plant growth regulators. Work being done is on a low level of effort, usually as a sideline of on-going R&D. Some companies are maintaining effort in juvenile hormones so that they will have gained sufficient experience when they feel the market is ready. Others look into these types of controls as part of their basic research, looking at different modes of actions in major pests. Some companies have been working in the juvenile hormone area, have decided it is not a profitable venture and are eliminating that area of research.

The most prevalent attitude towards naturally occurring biological control methods is the attitude of "vigilance." This is expressed in several ways, i.e., companies are "keeping track of what is going on" or "keeping up with the literature" or "leaving the door open for research in that area" but waiting to see how well others do in the business.

The lack of effort in the more innovative naturally occurring biological controls is due to several problems foreseen by industry in that area:

(1) The biggest problem seems to be lack of patent protection for bacteria and viruses. After a company has made large expenditures to register a bacteria or viruses it is faced with the possibility that other companies can then register the same bacteria or virus and undercut the price since they do not have to make up for registration costs. This is compounded by the fact that the active biological ingredients may be easy to make and thus the market is easily entered. BT, for instance, can easily be made by standard fermentation processes. This is further compounded by the fact that the entire market for BT presently is estimated at only two to three million dollars. (The market for viruses is still uncertain.) A dissenting opinion on the problem of patent protection is that the formulation of naturally occurring biological controls is a challenge in overcoming problems of stability, potency and reliability. A successful formulation which solves these problems can be patented and can be used to maintain a continuing place in the market. Others hope the 3(c)(1)(D) clause requiring the payment for use of registration information will supply some protection, and prevent some "me too" companies from entering the field.

According to some industry spokesmen, some biological controls developed by the government are currently sitting on the shelf because the lack of exclusive patent protection. If a biological control is discovered in the U.S.D.A. labs in Beltsville, Maryland, they are passed on to other U.S.D.A. labs for feasibility tests and then are available to industry to develop commercially. However, the lack of patent protection or non-exclusive rights to government developments causes many industries to hesitate in taking advantage of this opportunity. Some companies recommend that competitive bidding be used to provide exclusive rights to industry for biological control approaches discovered by government laboratories.

(2) The second major cause for lack of effort in the biological control field are problems in formulation stability and reliability that are causing the costs of development of naturally occurring biological controls to go up. Viruses, in particular, involve problems in stability and packaging. Companies involved with the development of viruses say that these problems of stability are a much greater influence on timing and costs of development than any registration requirements.

(3) Consumer acceptance is the third major problem in the biological control field. The consumer may not be willing to compensate for the added costs of development of these biological controls, or the added cost of any specialized application techniques. Even without these added costs, industry expects that a great deal of education will be required before the farmer will accept naturally occurring biological controls. For instance, controlling the sweet corn earworm with BT will assure that the earworm does not eat the corn but the consumer will find

enlarged diseased earworm still on the corn when it reaches the market. This is a general problem with BT since it does not eliminate the presence of the insect for several days, although it does almost immediately stop it from consuming the crop.

(4) Most companies feel that biological controls can only be used on a regional basis as part of the integrated pest control program. They expect that increased government management and control of pest programs will be necessary before biological controls can be used successfully. Some companies feel that only government programs such as that of the U.S. Forest Service represent viable markets for these controls, and they do not expect, or desire this amount of government control of private agriculture.

(5) Lastly, those companies which are not actively involved in biological control feel that EPA will and should be cautious about possible hazards to human health presented by naturally occurring biological controls, both BT and the viruses that are currently being investigated. The fact that the pesticidal mechanisms are not fully understood in these compounds is a cause for concern. Even the development of genetically resistant crops may involve chemicals which are present in the crop. These chemicals are unknown and untested and are transported directly to the consumer. Also, introducing viruses into the environment even in small plot field tests is felt to be less safe than chemical compounds since the viruses can propagate and thus cannot be removed from the environment via the usual method of destroying the crop. The general mistrust for naturally occurring biological controls on the part of many companies can be summarized by one R&D manager we contacted who stated, "I'd rather take a bath in DDT than stick my finger in BT."

IV. LEGISLATIVE ACTIONS AND THEIR IMPACT

A. INTRODUCTION

The United States is and has been committed by law, regulation, policy and tradition to insure that the food supply of the nation is safe, clean and wholesome and to protect the safety and health of the direct and indirect users of pesticides and the consumers of products which depend upon pesticide use. The quality of the total environment--soil, water and air--in which food is grown, processed and consumed controls to some degree the quality of our food and our health. Contamination of these natural resources by pesticides, their residues, and related materials not only affects the quality and safety of our food, but also affects environmental values such as wildlife preservation, recreation and aesthetics. Thus, the regulation and control of pesticide has broad influences over the public health, safety and welfare.

Federal regulation of pesticides began with the Insecticide Act of 1910; this Act was intended to prevent fraudulent efficacy claims and to authorize the seizure and banning of compounds dangerous to health.

The great increases in variety and use of synthetic chemical pesticides during and after World War II resulted in the passage of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) in 1947, a law designed to regulate the marketing of "economic poisons" and "devices." These terms were originally defined as "economic poison--any substance or mixture of substances intended for preventing, destroying, repelling or mitigating any insects, rodents, nematodes, fungi, weeds and other forms of plants or animal life, which the Secretary (of Agriculture) shall declare to be a pest and any substance or mixture of substances intended for use as a plant regulator, defoliant or desiccant." "Devices" were defined as "any instruments or contrivance intended for trapping, destroying, repelling or mitigating insects or rodents, or destroying, repelling or mitigating fungi, nematodes, or other pests, but not including equipment used for the application of economic poisons when sold separately therefrom." FIFRA was amended by the Nematocide, Plant Regulator, Defoliant and Desiccant Act of 1959, and amended again in 1961 and in 1964.

Under FIFRA (administered by the Department of Agriculture) pesticide chemicals could not be distributed or sold in interstate commerce unless they had been shown to be safe when used as directed and effective for the purpose claimed on the label.

Any residues remaining on food or feed could not exceed the safe tolerance level established by the Food and Drug Administration in implementing the Pesticide Chemicals Amendment and Food Additives Amendment of the Food, Drug and Cosmetic Act. The purpose of this Act was to insure the safety of the nation's food supply by requiring that the residues remaining on food were shown (by the industry wishing registration of the pesticide) to be safe for the consumer before the pesticide could be cleared for general use.

As pesticides came into ever-wider use, and their environmental as well as their health effects became known, the federal government began assessing and implementing the need for greater regulation of pesticides. A broad range of environmental concerns were addressed in 1970 through guidelines for studies to determine the impact of pesticides on the environment (PR Notice 70-15)--environmental data required as part of the application for registration. In December 1970 the authority to administer FIFRA was transferred to the Environmental Protection Agency as well as the authority to establish tolerance levels for pesticides and residues for food and food products. In October 1972, HR 10729, the Federal Environmental Pesticide Control Act (FEPCA) or "FIFRA amended" was signed into law. The implementation of FEPCA and its regulations is now proceeding in accordance with the requirements of the law.

In this section of the report, we will briefly discuss the major features of FIFRA and FEPCA, concentrating on those parts of the law and subsequent regulations which have the greatest potential effect on research and development activities in the pesticide industry. We will summarily compare FIFRA and FEPCA, to the extent definitive regulations have been promulgated.* Then we will address the specific and general impacts of these laws and regulations on research and development in the pesticide industry.

B. REVIEW AND COMPARISON OF FIFRA AND FEPCA

1. FIFRA

FIFRA provided for labeling which specified uses of pesticides with appropriate cautions and warnings and prohibited the interstate sale and/or shipment of economic poisons which were not registered, or were misbranded or adulterated. Further, it was unlawful for anyone to detach, alter or destroy pesticide labeling, to refuse to provide access to books and records authorized in the Act to persons designated by the Secretary, to provide false guarantees, or to use for his own advantage or to reveal (in general) information relative to formulas of products obtained through the registration process. FIFRA provided for the registration of economic poisons, and the suspension or cancelling of the registration of an economic poison wherever it appeared that the article or its labeling did not comply with the provisions of the Act. FIFRA also outlined the review and appeal process for registration. The law also called for maintenance of books and records on pesticide shipment and delivery by manufacturers, distributors and others involved in selling pesticides. Enforcement provisions were authorized as were penalties and seizure of illegal pesticides. Imports were regulated to provide for inspection to determine whether the products were adulterated, misbranded, or were dangerous to health. Reregistration of pesticides was to occur at five-year intervals.

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*Several notices of proposed regulations under FEPCA were published in the Federal Register during this investigation. We were not able to obtain information on industries' views of the impact on R&D of these recent changes.

Regulations under FIFRA subsequently defined the labeling process and label content, the procedure and requirements for registration, guarantees, coloration and discoloration, adulteration and misbranding and enforcement.

The principal parts of FIFRA which affected research and development activities in the pesticide industry were the regulations and requirements involving registration and labeling, the experimental use of pesticides, and the establishment of tolerances.

a. Data Required for Registration

For the Department of Agriculture the applicant for registration had to furnish documented proof to support the claims made for the proposed product. Data required to support registration usually included the following:

Toxicity Tests and Data

Toxicity tests on the proposed formulation were to be conducted to show that the directed use of the product would not be injurious to exposed man or beneficial animals when warnings and cautions are carefully followed. The extent of toxicological data required varied with the nature and proposed use of the product. Toxicity studies normally included:

Safety Data

- Acute mammalian studies (oral, dermal, inhalation, and eye and skin irritation).
- Subacute studies--oral - 90 days; dermal - 21 days; inhalation - 14 days.
- Other studies required in some cases included:

  Neurotoxicity
  Teratogenicity
  Effects on reproduction
  Synergism
  Potentiation
  Metabolism
  Avian and fish toxicity

Physical - Chemical Data

- Boiling point
- Flash point
- Physical state
- Density
- Vapor pressure
- Solubility
- Stability

Efficacy Tests and Data

Biological tests under field and laboratory conditions were to be conducted to show that the product would control the pests named on the label, when used as directed, without causing significant adverse effects to the crop or property being treated. The following factors were considered in determining efficacy:

- Effectiveness
- Phytotoxicity
- Translocation by the plant or animal being treated
- Persistence in soil, water or plants
- Compatibility with other chemicals
- A thorough search and evaluation of the data submitted as well as other applicable data

Labeling

General labeling requirements consisted of:

- Name of product
- Name and address of manufacturer, registrant, or person for whom manufactured
- Net contents
- Ingredient statement--name and percent (by weight) of each active ingredient, and total percent of ingredients
- Warning or caution statement--the label of any economic poison had to show warnings pertaining to:

    ingestion
    skin absorption
    inhalation
    flammability or explosion

- The registration number assigned to the product

- Directions for use which are adequate to protect the public

Other required information in the registration process included:

- Data to support any or all claims on the labeling
- A complete statement of the composition of the product, including the percentage by weight of each of the active and inert ingredients, if such information does not appear on the label
- Any pertinent information about inert ingredients
- Any other information pertaining to physical or biological properties of the product, etc.

Petitions for registration filed with the Department of Agriculture were reviewed and commented on by other departments of the federal government. The Department of Interior reviewed all petitions for registration of pesticides whose use patterns may have had an impact on fish or wildlife. The Public Health Service of the Department of Health, Education and Welfare, reviewed all petitions from the standpoint of human safety. The comments of these two agencies were then forwarded to the Department of Agriculture and were considered before registration was granted or refused.

Analytical method(s) suitable for enforcement purposes were to be provided with the petition if suggested use patterns would result in residues of the chemical on food or feed. The analytical method(s) and the residue levels presented in the petition were evaluated and an opinion on whether the proposed tolerance reasonably reflected the residue was forwarded to the Food and Drug Administration.

b. Establishment of Tolerances

If the product was proposed for use in a manner which was likely to result in residues in or on food or feed, the product was not registered by the Department of Agriculture until a tolerance or exemption had been granted by the Food and Drug Administration.

Tolerances under Section 408 of the Food, Drug and Cosmetic Act were established on raw agricultural commodities. The criteria and data requirements for establishing tolerances are summarized below. The basic requirement was that the data and other information furnished, when evaluated as a whole, established the safety of the proposed pesticide tolerance.

Chemical Data

The residue data must delineate the identity and magnitude of the residues and must show that, under the proposed conditions of use, the proposed tolerance is suitable.

The analytical methods used to obtain the residue data must be valid and must afford a measure of the total toxic residue.

Toxicological Data

The requirements for the two major types of tolerances--for negligible residues and for residues (higher levels) are outlined below:

(a) A negligible residue tolerance was one that was sufficiently limited by the magnitude of the residue, extent of use, and mode of use so that the levels of ingestion which result were considered to be of little or no toxicological significance. The safety factor (the ratio of residue level to level at which toxicological effects occur) was usually about 2000 based on 9-day toxicity studies.

(b) A tolerance for residues in excess of negligible residues required the following data:

Acute Toxicity

- LD_{50} in at least two species of animals
- A description of the signs of toxicity

Short-Term Toxicity (subacute toxicity)

- At least two species, one a non-rodent
- Duration, 90 days
- At least three damage levels plus a control group; one dosage level should be toxic
- When 9-day studies are designed to continue for long-term toxicity studies, sufficient animals must be started to supply the required number for the long-term studies
- Observations--growth, food consumption, general appearance and behavior, mortality, organ weights, clinical laboratory tests (blood, urine, organ function, enzymatic and metabolic) and gross and microscopic examinations
- In the case of organo-phosphorous and carbamate pesticides cholinesterase inhibition and demyelination studies were to be made

Long-Term Toxicity (chronic toxicity)

- At least two species, one a non-rodent

- Duration usually two years

- Tests and observations similar to those above for short-term toxicity

Biochemical Data

- Data from at least two species of animals

- Observations: absorption, distribution, metabolic transportation, elimination, possible accumulation, and the effect of enzymes which should be examined because of the nature of the chemical under study

- Information on metabolism of pesticides and their other conversion products in treated plants

Reproduction Studies

- At least one specie, preferably two

- At least two dosage levels, plus a control group

- Usually three successive generations in the rat; two generations are satisfactory if the results are conclusive

- Preferably two litters per generation

- Both the males and females should be treated for 60 days prior to breeding; the second and third generations were to be treated from weaning throughout the breeding period

- Observations: fertility, length of generation, live births, still births, survival at 4 days and at weaning, sex of newborn and of weanlings, body weights, gross abnormalties, and microscopic and skeletal examination of young in last generation

Data on Man

- From industrial exposure

- From accidental poisoning and suicides

- From controlled requirements in special cases

- Useful biochemical data of the type indicated above

Any additional studies that might be indicated by results of the studies above.

When the FDA established a tolerance, and the USDA requirements were met, a registration based upon the tolerance or no residue status was granted. Additional data was required for each use (crop or pest) that was indicated on the label.

Although the general requirements for registration were similar for all pesticides, amount of data required and the complexity of tests and results varied with the pesticide, its properties, and its proposed use. Frequently additional data were required as the initial tests were reported to USDA and suggested the need for more or confirmatory information.

c. Experimental Use Permits

Another important feature of FIFRA which affected research and development activities was the temporary permit program. Although FIFRA originally provided no explicit authority to regulate the experimental uses of pesticides, Section 7(a)(4) of the law provided the basis for subsequent regulations. Section 40 CFR 162.17 (amended 1964), provided for "temporary permits, not to exceed one-year period, for shipment of limited amounts of a product which is to be tested, usually on a larger scale, to determine its limitations." Permits were to be issued only for bonafide experimental programs under supervision of qualified persons. Permits were not required for substances that were being tested "only to determine their value for economic poison purposes, or to determine toxicity or other properties, where the user does not expect to receive any benefit in pest control from its use." Also an economic poison for experimental use by or under supervision of authorized federal or state agencies did not require a permit. Both general (multiple shipment over time) and specific (specific shipment and date) permits were issued. If tests were to be conducted so that residues could result on food or in feed, one of the following were required: data were required to show that no residue would be present, a tolerance or exemption from tolerance (permanent or temporary) had to be established by the FDA and data provided to show that the experimental use would not result in residues which exceed tolerances, or the food or feed derived from the experimental program had to be destroyed, fed to laboratory animals only, or otherwise safely disposed of. The permit application required certification of use of the food or feed, shipping information, composition, quantities, data on toxicity, description of the experimental program, percent of material supplied without charge and proposed labeling information. Quantities shipped could be limited and reports on the experimental program were required every three months. Experimental permits could be cancelled for violation or for the protection of the public. As a result of the implementation of this regulation, experimental permits could be easily and readily obtained and potential pesticides tested broadly on an experimental basis to gain research and development and marketing information for industry. Many R&D activities were under the direction of state and federal agencies (agricultural extension programs at universities) and no permits were required.

2. Changes to FIFRA

As indicated earlier, the data requirements of FIFRA evolved over the years from 1947 to 1971 at a slow but steady pace. Several major changes occurred which significantly affected the research activities of industry. Prior to 1966, pesticides could be registered with either a "negligible residue" or with a "zero tolerance" as provided for in the Federal Food, Drug and Cosmetics Act, Section 346a. As a result of advances in analytical techniques, and the growing realization that even small quantities of pesticide residues could have important health effects, a policy change was instituted in April 1966 that required re-evaluation and reregistration of pesticides with zero tolerance or no residues, and a finite tolerance was required for future registrations. USDA and FDA agreed that then current registrations should be discontinued after December 31, 1967 unless producers presented evidence to support a finite tolerance or to show that progress was being made on work leading to such evidence. Products which were being reregistered (every 5 years under FIFRA) required additional data to support these new tolerance requirements. It was the intent that no pesticide registered after January 1971 would have a zero tolerance or no residue as the basis for registration. As discussed later, this change led to additional research and development to assure continuation of registration of existing products as well as to obtain registration of new pesticides.

A second major change occurred as a result of PR Notice 70-15, June 23, 1970, in which the Dept. of Agriculture posed the following basic questions to be answered in support of registration of pesticides.

- What is the rate of dissipation of the pesticide in the soil?
- What is the mechanism of degradation of the pesticide residues?
- Do the residues leach through the soil?
- Are the residues moved from the site of application by runoff water?
- Is the pesticide bound in soils, that is, are residues present that are not readily extractable?
- What levels of the parent compound and principal metabolites will accumulate in fish, rabbit, and bird tissue and what dosage related symptoms are exhibited during the laboratory test period?

The data and studies required to answer some of these questions varied with the compound, its proposed use, toxicity, and the details of the registration review process at the time the application was submitted.

A third factor which influenced the research and development activities related to FIFRA was the Delaney Amendment to the Food, Drug and Cosmetic Act (Title 21, Section 348(c)(3)(A), October 1962), which effectively prohibited the existence of pesticides or their residues in any measurable quantities on food if the pesticide or residue was a known carcinogen. Additional test efforts were required (described earlier) to determine the carcinogenicity of pesticides and their metabolic products.

3. FEPCA

The FEPCA, or frequently referred to as "FIFRA, as amended," contains many new provisions and is in the process of being implemented in the period from 1972 to 1976. Only a portion of the expected regulations and policies under FEPCA have been proposed or promulgated and the impacts of the anticipated regulations are unclear. Nevertheless, there are changes in the law which may impact R&D activities.

The registration requirements under FEPCA are very similar to those under FIFRA. However, one major difference is that all pesticides shipped, sold, delivered and received, both inter- and intra-state, must be registered unless it constitutes an internal shipment from one registered establishment to another operated by the same producer for packaging or as a constituent of another product, or unless it is covered by an experimental use permit. Another difference is included in Section 3(c)(1)(D) which requires that the Administrator may not consider the test data supporting one application in support of another application for registration, unless the second applicant has first offered to pay reasonable compensation for test data and that the test data is not protected from disclosure (e.g., information designated as trade secrets). If the parties cannot agree on an amount and method of payment, the Administrator shall make that determination, with an appeal procedure specified.

Guidelines specifying the kinds of information required in support of registration are to be published and revised from time to time. At present, several draft versions of these guidelines have been informally issued. Most of the data requirements are similar to the latter stages of FIFRA. Some additional requirements are being added as part of the evolutionary process of learning more about the environmental and health effects of pesticides.

The Administrator is to review the data in the application as expeditiously as possible and either register the product or notify the applicant that registration is denied. After receipt of the application and the required data for a pesticide with a new active ingredient or a changed use pattern, a notice of application must be published in the Federal Register providing for 30 days for any federal agency or interested person to comment. The pesticide shall be registered if:

- its composition is such to warrant the proposed claims,

- its labeling complies with the requirements,

- it will perform its intended function without unreasonable adverse effects on the environment, and

- when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.

The law specifically states that the Administrator shall not make any lack of essentiality a criterion for denying registration and indicates that when two pesticides meet the requirements above, one should not be registered in preference to another.

Registered pesticides will be classified as either for general use, restricted use, or both, with specific directions and clearly distinguishable packaging and labeling for general and restricted uses. A pesticide will be classified for general use if it will not generally cause unreasonable adverse effects on the environment. A pesticide will be classified as restricted because of its potential for harm to the applicator or unreasonable adverse effects on the environment. If a pesticide is designated restricted because of hazards related to acute dermal or inhalation toxicity, the pesticide may only be applied by or under the supervision of a certified applicator. (Applicators are certified by states under plans approved by the Administrator, according to standards for certification prescribed by the Administrator. These standards are to be issued by October 1975.) If a pesticide is classified as restricted because of possible unreasonable adverse effects on the environment, it can only be applied by or under the supervision of a certified applicator and may be subject to other restrictions by regulation (with an appropriate appeals procedure). The classification of a pesticide may be changed with the accompanying notification of the registrant and publication in the Federal Register. If the Administrator denies registration of a pesticide, the denial and reasons therefore must be provided to the applicant and published in the Federal Register.

Section 5 of FEPCA calls for application and issuance of experimental use permits to allow the applicant to obtain information necessary for registration of a pesticide. A temporary tolerance level is to be established (if required) before issuing an experimental use permit; studies may be required to detect whether a new pesticide may cause unreasonable adverse effects on the environment when used under an experimental permit; experimental use permits can be revoked by the Administrator, and the Administrator may authorize states to issue an experimental use permit for a pesticide.

Several new provisions for cancellation, change in classification, and/or suspension of the registration of a pesticide or hearings to determine a course of action are provided for in the law. These processes are to occur if: the registrant does not request continuation of the registration after a five-year period; if the pesticide or its labeling does not comply with the provisions of the Act; if the use of the pesticide in accordance with widespread and commonly used practice generally causes unreasonable adverse effects on the environment. Hearings, emergency orders, public hearings, scientific review and judicial review are also delineated.

The law calls for registration of establishments in which pesticides are produced and submittal of data on the types and amounts of pesticides produced.

As under FIFRA, books and records of pesticide production operations movement and shipment are to be kept and made available to EPA staff designated by the Administrator. FEPCA contains a number of new provisions which enhance the federal enforcement capability. Both civil and criminal penalties are authorized. Authorized representatives of the Administrator may enter pesticide establishments or other location of storage or sale of pesticides for the purposes of inspection or sampling, after giving appropriate reasons for the inspection. A number of new unlawful acts were added to FIFRA, including the use of any registered pesticide in a manner inconsistent with its labeling. Stop sale, use or removal orders are authorized, and products in violation of the Act may be seized.

The administrative and judicial review procedures are clarified, and restrictions to pesticide imports and exports (similar to FIFRA) are provided.

Several other important points of the law (with regards to possible impact on R&D) include the provision for indemnity payment to certain persons who suffered losses by reason of suspension or cancellation of a registration. The Administrator is to establish procedures and regulations for the disposal or storage of pesticide packages and containers, and to establish packaging standards. The Administrator also shall undertake research as necessary for the purposes of carrying out the Act, and give priority to research to develop biologically integrated alternatives for pest control. Under Section 24, a state may provide registration for pesticides formulated for use within its bounds, if it has been certified by the Administrator to do so.

As with FIFRA, the implementation of FEPCA will evolve as new regulations are promulgated, with a schedule which extends through 1976. Guidelines for data requirements for registration have been drafted and may soon be issued. Criteria for classification of pesticides have been drafted and announced recently. Regulations for registration of pesticide-producing establishments, submission of reports, and labeling were issued in November 1973. An interim policy for the administration of Section 3(c)(1)(D) was issued in November 1973. Proposed regulations to establish standards of competence for applicators of pesticides were issued in February 1974. Revised proposed procedures for the use of pesticides for experimental purposes were issued in March 1974. Many of these recent proposed regulations are now receiving comment from the public prior to their promulgation.

4. Comparison of FIFRA and FEPCA

It is not appropriate to compare FIFRA and FEPCA on a section by section basis because FIFRA evolved over a 25-year period and many of the anticipated regulations and guidelines under FEPCA have not yet been issued. Further, many of the regulations and provisions concern administrative processes and have only a secondary impact on R&D activities, if any. In this section we will present a brief time analysis of portions of FIFRA, showing major changes, and then compare the principal features of FIFRA and FEPCA which may influence R&D activities.

Table 8 shows the evolution of the principal regulatory actions and policies and the changes in data required (primarily for registration) over the 25-year period after passage of FIFRA. The exact dates for the implementation of the regulations and policies is generally unimportant since the impacts caused by the changes in regulations and data requirements have been gradual.

The most significant changes in FIFRA, as determined from our discussions with industry, were the change in residue data requirements, addition of environmental data requirements and overall continued requests for more precise and extensive health and environmental data.

Table 9 compares the principal features of FIFRA (at a time just prior to FEPCA) which affect R&D activities with similar features of FEPCA (at the present).

	1947	1952	1957	1962	1967	1972
Law	Enactment of FIFRA		Amendments to FIFRA	Delaney Amendment to Food, Drug and Cosmetic Act		FEPCA
Regulations	Development of Regulations and Their Implementation		Amendments, Changes and Interpretation of Regulations		PR 70-15 Requirements for Environmental Data	Regulations for Implementation of FEPCA
Policies	Priority on Efficacy and Prevention of False Claims		Priority on Efficacy and Increasing Importance on Human Safety	Environmental Priorities Increasing	Priority on Assuring No Unreasonable Adverse Environmental Effects (including health)	
Data Requirements	Modest Data Requirements Under Initial Implementation		Increasing Requirements for Toxicity and Efficacy Data	Added Carcinogenesis Data Requirements	Changes in Tolerance and Residue Requirements	Added Environmental Data Requirements From PR 70-15, e.g., variety of species, bioaccumulation, degradation products, etc.
Administration	Jointly by USDA, FDA, Dept. of Interior with Other Agency Comments ⟶				Administration of FIFRA by EPA ⟶	Administration of FEPCA by EPA

TABLE 8. TIME FRAME FOR CHANGES IN FIFRA

TABLE 9. BRIEF COMPARISON OF FIFRA AND FEPCA

	FIFRA	FEPCA
Administration	USDA, FDA and Dept. of Interior from 1947-1970; EPA from 1970	EPA with input from other agencies
Registration Requirements		
Applicability	Pesticides in interstate commerce. Pesticides "for experimental use only" excluded.	Pesticides in inter- and intrastate commerce. Pesticides "for experimental use only" excluded.
Procedures	Statement to be filed with name of pesticide and applicant, labeling including claim and directions for use, description of tests and results, if requested.	Statement to be filed with name of pesticide and applicant, proposed labeling, including claims and directions for use, formula, description of test and results, if requested, offer to compensate for use of data, request for general or restricted use classification.
Data Required	Toxicity and efficacy data including residues and metabolites with early emphasis on human health and product performance; environmental data added later, generally increasing requirements with time, data requirements vary with product and proposed use.	Generally similar data to FIFRA just before FEPCA with some further increases; apparently some unspecified requirements, guidelines not completed, data requirements vary with product.
Approval of Registration	Approval granted if tolerance established by FDA (if needed) and USDA requirements met.	Approval granted if composition warrants claims, meets requirements of Act, will perform intended function without unreasonable adverse effects on the environment, in normal use will not generally cause unreasonable adverse effects on the environment.

<table>
<tr><th>FIFRA</th><th>FEPCA</th></tr>
<tr><td colspan="2">Cancellation of Registration</td></tr>
<tr><td>Suspension or cancellation procedures when pesticide is in violation of the Act with appropriate review appeal process. Cancellation after 5 years unless continuation requested by registrant.</td><td>Similar, but somewhat stronger, suspension and cancellation procedures, including stop sale, seizure, emergency order, etc., provisions. Public hearings, scientific review and appeal process. Cancellation after 5 years unless continuation requested.</td></tr>
<tr><td colspan="2">Classification of Pesticides</td></tr>
<tr><td>No classification under FIFRA.</td><td>Classification of pesticides as general use, restricted use, or both. Changes in classification provisions.</td></tr>
<tr><td colspan="2">Certified Applicators</td></tr>
<tr><td>Not required under FIFRA.</td><td>Restricted use pesticides to be applied by certified applicators only; applicators to be certified by states in accordance with standards set by Administrator.</td></tr>
<tr><td colspan="2">Books and Records</td></tr>
<tr><td>Records of delivery, movement of pesticide, etc., to be provided to authorized person on request.</td><td>Similar to FIFRA with additional requirements for registration of establishments which produce pesticides and data submittal.</td></tr>
<tr><td colspan="2">Use of Data</td></tr>
<tr><td>Administrator not constrained from using efficacy or effects data from previous applications as basis for acting on other applications. No compensation for use of data.</td><td>Applicant must agree to pay reasonable compensation if others' test data are used in support of registration application. Provisions for protection of trade secrets in law.</td></tr>
<tr><td colspan="2">Unlawful Acts, Enforcement and Penalties</td></tr>
<tr><td>Specification of unlawful acts, provisions for enforcement, including sample collecting, etc., and assessment of criminal penalties.</td><td>Similar unlawful acts strengthened enforcement provisions, including civil and criminal penalties, sampling and inspection and prohibiting use of pesticide except as specified on label.</td></tr>
</table>

	FIFRA	FEPCA
Experimental Use Permits	Required for experimental use of non-registered pesticides except under supervision of federal and state authorities. Temporary tolerance may be needed. Modest toxicity data needed. Quantities limited, reports required, general retail sale prohibited.	Required for all experimental use of non-registered pesticides, temporary tolerance may be required. Increased data requirements for permit. States may issue experimental permits, if authorized, limitations on acreage, resale prohibited, increased notification and records of shipment and use, etc.
Storage, Disposal and Packaging	Pesticides subject to packaging standards set by HEW under Poison Prevention Act.	Administrator to establish procedures and regulation for storage and disposal of pesticides and containers. Administrator to set packaging standards to protect persons from serious illness.
State Functions	Responsibility for manufacture and use solely within state.	May regulate sale or use within state; shall not impose additional or different labeling or packaging requirements; may provide for registration of pesticides for distribution and use within state for local needs if certified by Administrator; certify applicators according to federal standards.
Indemnity	No provisions.	Indemnification for certain persons suffering loss as a result of suspension and cancellation of registration.
Research	No specific research provisions.	Administrator to conduct research to aid in implementation of Act with priority on biological controls.

C. SPECIFIC IMPACTS OF LEGISLATIVE AND REGULATORY ACTION

1. Introduction

The changes which have occurred in the research and development activities of the pesticide industry in the past 25 years can be attributed to many factors--new agricultural policies, development and improvement of farming methods, changes in the general economy, development of international markets and balance of trade considerations, farm labor supply and demand, technological advances, environmental awareness of the public, attitudes toward public health and safety, availability of raw materials for organic synthesis and federal and state regulatory actions. The relationships among these factors are complex; there have been many factors which act in concert to bring about a new direction or trend in research such as the specialization in research on herbicides by a particular organization or the initiation of a biological control research program. The trends in research and development activities have been described in Section III. Here we will attempt to identify and describe the impacts of specific regulatory actions on pesticide research and development activities. In Section D we will relate general trends and changes in research and development activities to combinations of regulatory actions and other factors not directly influenced by pesticide laws or regulations.

The format used for this section will be to state the specific impact or general change noted and then discuss the reasons for the impacts and other possible alternative views. The impacts, reasons, and alternative views are based primarily upon information and data provided to us in discussions with industry under this contract, and secondarily on published information and our own interpretation of the research and development activities and market structural elements of the pesticide industry.

2. Data Required for Pesticide Registration

The steadily increasing requirements for data on health, safety and environmental effects of pesticides in order to obtain registration have significantly increased the cost and time frame for pesticide registration and development by industry and have resulted in a decrease in the growth rate of innovative research and development activity. These costs and delays are balanced by the greater understanding of pesticide effects, derived from the registration data, and by the registration of effective, safe and environmentally sound pesticides.

When FIFRA was first enacted, the principal emphasis in the required data was to demonstrate the efficacy of the pesticide. As the use of pesticides became more widespread and as the public became more informed on health effects, steady increases in the data required for registration occurred. Toxicity testing became more important; more data were required to substantiate claims of efficacy, lack of damage to food crops, and lack of residues on food and in the soil. The duration of required tests was increased, and as analysis methods became more sensitive and sophisticated, the requirements for more accurate and precise measurements of toxicity, residues, metabolites, etc., were increased. The era in which the registrant could "walk the application through the registration process" came to a close. Data requirements under FIFRA were provided by USDA to applicants, however changes in requirements were frequent, and the quantity of data required increased as knowledge of health and environmental effects improved. Although general data requirements were the same for all pesticide applications, there was considerable flexibility on the part of the USDA reviewers to ask for more or less data depending upon the type of compound and the past experience with related compounds. Communication channels between industry and the regulatory agencies could be described as good, and industry generally felt that USDA was an ally to the producer as well as a regulator.

According to industry, a significant impact on data requirements resulted from the policy change in 1966-1967 which called for more extensive and sensitive residue data when pesticides were registered or reregistered. Several companies reported to us that "from 1967 to 1970 we essentially shut down our innovative research to obtain the required safety data." Other companies acknowledge the change, but indicate that it was not unreasonable, and "would have come along anyway" as a result of increased health concern as well as because of improvements in analytical methods. Data requirements continued to increase, with the next major impact resulting from PR 70-15 which added significant new data on environmental impact and the fate of pesticides in the environment. Some pesticide companies believe that the shift in emphasis from efficacy and human health to environmental concern represented the greatest change in data requirements and the greatest impact on cost and timing of the registration process. The reasons given include the "new type of data required, the development of new analytical methods, needs for tracer studies, different type of staff required, larger dimensions of the animal studies, sequential requests for additional environmental data, etc."

Another important factor mentioned by several companies was the gradual increase in data required to show definitely the absence of health effects such as carcinogenicity, mutagenicity, teratogenicity, etc. Some industrial sources attribute the major increase to the Delaney Amendment, others to public pressure and federal response in terms of data required for registration. The principal impact of the tests needed to obtain these data was not primarily the added cost, but the time required to conduct the studies. The two-year period for carcinogenicity tests lengthened the overall process of development, even though most companies conduct this work at the same time as they are doing other studies of similar long duration. Industry considers the two-year duration as almost a three-year test period, when planning, analysis, reporting of the results are included.

Although the guidelines for data in support of registration under FEPCA have not been formally issued, drafts of the guidelines have been circulated both within and outside EPA to industry. From discussions with industry staff who have reviewed these guidelines, we conclude that there are few major changes in types of data required for registration under FEPCA, but that the quantity of information needed continues to grow as before. This continued increase requires additional R&D efforts and can detract from more innovative development of new and better pesticides.

In our discussions with industry, we were provided with many examples of the impacts--delays and costs--to industry which were attributed to data requirements for registration. Most of the comments, and complaints, were based upon histories of registration of specific products, or particular problems which each specific company encountered. In the next few paragraphs, we will generalize these specific comments and report those suggestions of industry in terms of data requirements and accompanying registration procedures.

Industry's views of the data requirements for the registration process fall in two categories--technical considerations, including the relevancy, significance, methodology and necessity of various tests--and procedural considerations. Most companies agree that the technical aspects of the tests and required data are costly, time-consuming, and detract from other areas of R&D. However, they also agree that, for the most part, these tests and data are necessary to provide scientific basis for registration of pesticides to assure health and safety to man and the environment. A frequent comment of industry is: "many or most of the tests required by EPA must be conducted by industry in product development (even in the absence of regulatory action) to assure that the product can be successfully marketed and to insure that the product is safe, i.e., protect the company from possible litigation." Industry, on the other hand, feels that all tests required for registration need not necessarily be conducted on all products and that better use should be made of past data from similar tests with the same or related products on similar or related crops. Industry questions the necessity and relevancy of some of the questions asked by EPA reviewers in the reviews of registration applications, particularly those questions which relate to the fate of the pesticide in the environment, analysis and tracing of decomposition products. The tests in this area of study are some of the most costly and time-consuming, and the results can vary considerably depending upon environmental conditions. Furthermore, the tests require the development of new, sensitive analytical methods, and multiple test areas.

A problem exists in that, on one hand, industry would like to see test requirements made specific and relevant to particular products and crop or insect usages, i.e., leading to flexibility in test requirements among products. On the other hand, a portion of industry would like to have the data requirements for all products and usages carefully defined so that they "know how to proceed" and could thus count on a more straightforward registration process. Clearly a compromise must be accepted in which certain requirements must be identified for all products and others must be dependent upon the product, use, and judgment of the EPA reviewers.

Other, more specific technical problems noted by industry in the data required for registration which have added to the cost and time of pesticides R&D include:

- Requirements for the development of new analytical techniques;
- Increased numbers of species for animal tests, including some which are difficult to use;
- Breadth and possible duplication of tests needed for mixtures of pesticides;
- Accuracy requirements for product content in low strength product formulations;
- Difficulty in conducting tests on aquatic herbicides; and,
- Possible requirements to use ASTM specified test methods which may not be the most desirable or cost effective for particular products or research facilities.

Despite these technical problems, industry generally recognizes the inevitability that the data required for pesticide registration will continue to increase and that industry is competent and capable of dealing with the technology.

The procedural aspects of the registration process also affect the data requirements and thus have an impact on R&D. In fact, the procedural aspects of the registration process generally draw more criticism and concern from industry than the technical aspects, although it is difficult to determine whether the impacts on R&D are greater because of technical or procedural problems. The "absence of definitive registration guidelines," "inconsistent and serial data demands at the discretion of the individual reviewer,""lack of communication between applicant and reviewer and lack of disclosure to industry of changes in data requirements," "delays in the review process by EPA" are typical of industry comments. The principal impact of these problems on R&D include:

- Increased time required for the registration process;
- Increased staff needed to meet and handle procedural requirements;
- The diversion of R&D efforts away from the discovery and initial development of other new compounds;
- The cost of the added data; and
- The loss of income both in the near-term because of delays in product sales and in the long-term because of the reduction of time in which the company has a proprietary position.

From our discussions with industry and EPA, some of the comments seem to be justified but may be caused by the lack of EPA staff in the registration (and criteria and evaluation) areas needed to process the increased amount of work. Many of the procedural problems will be resolved in time with the acquisition of EPA staff, with the issuance of registration guidelines with reasonable provisions for changes and information flow to current applicants, with the successful implementation of the product manager program at EPA, and with the resolution of problems related to regulations and guidelines in other areas related to data--experimental permits, 3(c)(1)(D), etc.

Concerning the impact of registration data requirements on R&D activities in biological control methods, there is some disagreement among the few industrial proponents of biological controls. One faction suggests that biological control approaches have been "separated" from others in terms of data requirements in the registration and review process and should not be; such separation leads to a greater degree of caution by EPA and further data demands. Others question the validity of some of the required tests, indicating that they are too extensive in view of the specificity of the compounds considered. Guidelines for registration with specific considerations and interpretations for those biological approaches that are very different from traditional chemical approaches are needed. There are sufficient technical problems in the development, storage, application, and use of biological control methods which occupy the efforts of industrial R&D, so that there are only few compounds or approaches at the registration stage where they can be significantly impacted by EPA data requirements. For these few, however, procedural problems in EPA are probably more significant than technical problems.

There are several other types of positive and negative impacts of the data requirements for registration on industry. As a result of the test requirements, the research process in industry has been streamlined and made more efficient in certain areas. Earlier decisions are being made on whether to pursue specific compounds, and the screening processes have become more effective. Pesticide research groups have tended to specialize in certain areas, and to use outside contractor help in others. Typically, even major pesticide research organizations will have toxicity tests, bioconcentration studies, metabolism studies, carcinogenicity, teratogenicity tests, etc., done under contract with research laboratories that specialize in these areas. This is often done in order to reduce costs and maintain staff levels yet retain control over critical areas in the R&D process that are efficacy, field test or marketing oriented. Some companies have begun to contract some of the screening operations as well. As a result of the added data requirements for registration, much more information is available on the behavior and fate of pesticides in the environment at early stage, which hopefully can be utilized to prevent long-term adverse environmental effects.

The potential impacts of increased data requirements for registration, described above, are based upon industry's initial views of how Section 3 of FEPCA would be implemented. After data were collected for this report (Spring 1974), additional and far-reaching regulations and guidelines have been developed and/or issued by EPA pertaining to registration requirements and classification of pesticides. These guidelines and regulations could have additional potential impacts which are not addressed here.

3. Experimental Use Permit System

The proposed experimental use permit system will increase costs, timing and risks in pesticide research and development activities. Industry will challenge the proposed regulations unless a method is found to obtain the necessary use and marketing data.

a. Permits Under FIFRA

FIFRA provided a basis for the issuance of permits for shipment of pesticides. The temporary permit system under FIFRA is described under paragraph 362.17 of Title 7, Ch. III, Regulations for Enforcement of FIFRA. The principal features of the system were:

- Permits issued for one year for shipments of products in limited amounts for bonafide experimental programs only;
- Purpose of permit was to authorize tests to determine pesticide limitations;
- Information and data on products and test programs necessary to protect the public may be required to be submitted;
- Permits were not required if the test purposes were only to determine the value as an economic poison, or to determine toxicity or other properties and were of no benefit in pest control to the user;
- The pesticide could not be offered for general retail sale;
- Permits were not required for experimental use of pesticides under the direction of federal or state agencies;
- A tolerance, exemption from tolerance, or temporary tolerance or temporary exemption was necessary if the pesticide may cause residues in or on food or feed or if the food or feed derived from the program was not destroyed or disposed of in a manner which protects the public;
- Data required with the permit application included: statement of nature of the program, states and geographic areas used, previous test results, proposed labeling, amount supplied without charge, approximate quantity and dates or time period of shipment, data on toxicity, etc.;
- The quantities of the pesticides covered by the permit could be limited if information or effectiveness or hazards were insufficient to justify the scope of the work;
- Reports were required on a three-month basis.

The temporary permit system was used widely by commercial pesticide developers for several reasons:

- To obtain data on efficacy, application rates and methods, effects of environmental and geographic variables;
- To provide a means for obtaining data for registration--environmental fate, residues, decomposition, behavior of pesticides in the soil;
- To obtain marketing information--acceptance by farmer, distributor, user information, comparison with competitive products.

The information gained from the experimental field tests was integrated by the commercial developers into a decision-making process which resulted in stopping research and development on certain compounds and the continuing or accelerating research and development of others. Industry concensus is that only one or two compounds out of ten used in extensive field studies went into full scale development.

Several modes of operation were employed in the temporary permit system. Many companies operated their own farms over which they had complete control of the food or feed derived from the experimental program or had long-term leases on land used for experimental purposes. Others used distributors, formulators, food companies or independent farmers to manage and conduct the field work on their own farms and report the results of the programs to the pesticide developers. Still other pesticide developers would contract field test work to independent farmers, in addition to, or instead of the use of their own farms. There was extensive cooperative effort with universities, state colleges, and state and federal agencies for field testing. This latter work did not require the temporary permit and provided the opportunity to obtain data in other locations and on other crops or insects for use in registration applications. This system provided considerable flexibility for the commercial developers in several ways:

- They could obtain both market and performance data to assess the effectiveness and marketability of the compound in different climatological and weather conditions in various parts of the country;
- They were not necessarily committed to the operation of their own farms with the attendant capital and operating costs; and
- They could relatively easily follow the insect or weed problems in various locations.

The system was believed to build distributor loyalty as well as prepare the distributor for ultimate sale of the product. Initial contact with the farmer through the distributor--one of the main determinants of market practices--was felt to be essential to determine the potential for the various compounds. The data required for the experimental permit were relatively modest, at least compared to full registration. The time required to get a permit application approved was between about 3 to 6 months, if sufficient work had been done to obtain a temporary tolerance (if necessary). The pesticide developers and the regulatory agencies all recognized the need for the field test portion of the pesticide development process; the temporary permit program provided some measure of control to insure that the health and welfare of the public were not being compromised by the testing programs under the permit system.

The relative "looseness" of the regulations, and the ambiguity of some of the terms and provisions, was in part responsible for indiscretions and violations on the part of several pesticide developers. In some cases, relatively large quantities of "experimental use" pesticides were sold, and indeed the user obtained considerable benefit in pest control while the developer was obtaining market and efficacy data. Despite the occasional high volume sale of specific experimental pesticides by some companies, much profit could not have been realized by these companies because of the relatively high unit price of the pesticide at this stage of development compared to the price at final full production. Nevertheless, any income was welcomed by industry to offset the development cost.

b. Permits Under FEPCA

With the passage of FEPCA, the emphasis in the experimental use permit system seems to have shifted from efficacy and safety to environmental impact. Section 5 of FEPCA provides that any person may apply for an experimental use permit for a pesticide and that the Administrator may issue one to allow the applicant to accumulate information necessary for pesticide registration. The requirements for temporary tolerance is similar to that under FIFRA. Additionally, the law specifies that studies may be required to determine whether the pesticide used under the permit may cause unreasonable adverse effects on the environment, that experimental permits can be revoked, and that the states may issue experimental permits if authorized.

The proposed regulations for experimental use permits under FEPCA (Fed. Reg. Vol. 39, No. 60, March 27, 1974) represented a substantial departure from previous regulations. Since the publication of the proposed regulations, comments have been provided by interested parties to EPA, and the proposed regulations are under review. In this report, we do not feel it is appropriate for us to comment on the legality, wording, emphasis, or reasonableness of the proposed regulations, but rather to: (1) identify the principal changes in the regulation, (2) summarize some of industry's objections to these changes, (3) provide information on industry's views of the likely impacts on R&D if the regulations are promulgated and implemented as originally proposed, (4) present our views of possible impacts, and (5) make several recommendations or suggest possible alternative methods of implementation.

c. Changes in the Regulations

The principal changes or new regulations with regard to experimental permits as proposed under FEPCA are:

- Pesticides may be sold and distributed only to participants involved in the experimental program and are not for resale or other retail sale or other distribution.

- Exceptions to the permit system include pesticides used in screening tests in which the only purpose is to determine if they have value for specific pesticidal purposes and from which the user does not intend to receive any benefit from pest control from their use. These tests are limited to laboratory and small plot replicated field tests less than 10 acres by federal or state agencies, universities or commercial developers on areas leased or owned by them and continually operated as an experimental farm on a long-term basis, where the crop or test subject is destroyed or suitably disposed of.

- The permit application calls for: detailed description of the proposed test program, the crops, fauna, flora, sites, modes and situations of pesticide application, number of acres for test, name and address, etc., of the person responsible for day-to-day administration of the program as well as the participants in the program.

- The data required for the application include: composition of formulation by name and weight, chemical and physical properties for each ingredient including manufacturing processes and analytical methods, rates of decline of residues on the treated crop or environmental site. Biological data are required including the description and results of known testing to determine toxicity and effects on species at the site of application, adverse effects to non-target species, and adverse effects on the environment. Toxicity tests and data relevant to users and other exposed persons must be provided.

- Those awarded permits must supervise the test program, evaluate the results and report immediately any adverse effects.

- Provisions for entry of authorized persons to the test area for inspection and compliance are included.

- Labeling provisions are changed to include almost all information required on permanent label.

- Notification of shipment by applicant to the Administrator must occur at the time of shipment including amount of each shipment.

- Revocation procedures with provisions for hearings are prescribed.

- The regulations do not exclude federal and state agencies from the requirements for an experimental permit.

- Processing of permit applications will require at least 90 days.

d. Industry's Objections

Industry has raised strong objections to the regulations as initially proposed; most of these have been submitted in writing and are publicly available. In our discussions with industry, we were informed by many companies that the proposed experimental use permit program will have more serious changes from FIFRA to FEPCA. The objectives were based on early industry assumptions of how the regulations pertaining to Section 5 would be implemented. Since this time (Spring 1974) the proposed regulations on the experimental use permit program have been reviewed at EPA; some of the objections, summarized below, may have changed in light of the currently proposed regulations. The principal objections run the gamut from procedural to operational, to technical (in terms of data requirements), to philosophical.

The procedural objections include:

- Anticipation that publication in the Federal Register of applications for permits will include disclosure of chemical, structure, etc., resulting in premature disclosure of research efforts and potential products.

- Requirements for more complete labeling may be unnecessary, only emergency information and warnings since this may again disclose information prematurely.

- Additional paperwork is involved, e.g., anticipated daily reporting of shipments.

- Inspection of field studies is desirable but needs to be scheduled to avoid inconvenience to participating farmers.

- Expectation that extensive cooperation with the states and EPA regions will be required.

- Minimum of 90 days review of application is expected to yield scheduling and other problems since the experimental programs must be conducted within limited seasonal time frames.

Operational objections include:

- Exclusion of resale will prevent participation of distributors, formulators and others from permit programs and limit contacts with farmers, etc.

- Requirements for small tests on owned or long-term lease property for continual use as experimental farms are believed by industry to be impractical, costly, and unnecessary.

- Specification of the exact location of the test program may not be appropriate, particularly for tests on certain pests.

- Anticipation that state and federal agencies (and universities and agricultural colleges) will need permits for most of their work.

Technical objections include:

- The data requirements for the permit are extensive and out of proportion to the possible effects of the experimental use (particularly if quantities are limited by the Administrator).

- Toxicity data is felt to be appropriate, but environmental requirements anticipated are unreasonable. (The common complaint is that a "Catch 22" situation exists where the experimental use permit is needed to do the tests required to obtain the data for the permit application.)

Philosophical comments include:

- There is very little difference between the requirements for registration and for the experimental use permit under the proposed experimental use permit regulations. Is this the purpose and intent of the permit program?

- Is it appropriate to make special provisions for innovative pest control methods and can this be done so that it is not discriminatory?

- The proposed regulations make it mandatory to go through the experimental permit program in the process of developing a pesticide. Is this necessary?

e. Potential Impacts of the Proposed Regulations

It is not possible to identify in quantitative terms the potential impacts of the proposed experimental use permit program since this depends on the final regulations promulgated and the implementation procedures involved. Nevertheless, we can present, and comment on, several anticipated impacts and some of industry's reactions in terms of research and development activities.

- Increased cost of R&D--the cost of the research and development process will increase for several reasons. First, more research will be required to obtain data necessary for the experimental use application. Although these data can ultimately be used in the registration application, only a portion of pesticides which enter the experimental permit stage are commercialized, so that the total expenditures for all compounds (those which succeed and those which fail) will increase. Second, a larger number of research and development staff will be needed to follow and manage the experimental permit program. The unavailability of sites for the test program in various parts of the country, through agricultural research facilities and other organizations, will require that pesticide developers own or lease more land for continued experimental purposes, or spend more time obtaining cooperation from a greater number of participants. One major company estimated that the cost of additional land for experimental use will amount to more than $2,000,000 and that this will allow them only to work on about 10 major crop species in their tests. There is anticipation that the quantities of pesticides that can be sold under the permit program will be greatly reduced because of resale prohibition and loss of use of contract farmers, etc. This will cut back any return now provided to offset the R&D cost.

The increased R&D cost could result in several impacts: (1) the cost will be passed along to the consumers of those pesticides that are eventually registered and marketed, (2) the increased experimental use permit costs will result in more emphasis on other uses of registered products and decrease in innovative research, (3) the number of new products reaching the market will be decreased.

- Changes in timing of the R&D process--there are two principal impacts on the timing of the R&D process that can result from the implementation of the proposed experimental use permit regulations: (1) increase in overall length of the pesticide development and registration process and (2) shifting the order and scheduling of the R&D activities. Current industry experience indicates that an average of 7 months may be required for obtaining an experimental permit under present FIFRA requirements (prior to recent proposed experimental permit regulations). The duration depends upon what is considered as "obtaining the permit," i.e., once the application for permit has been submitted, it may take only 3 or 4 months to obtain EPA approval; if more data are required by EPA or if obtaining original data is considered as part of the duration, then clearly the process can require 6-18 months depending upon the level of detail of data need with the application. This level is not clearly defined in the proposed regulations, but is left to the discretion of the reviewer and the Administrator by necessarily open ended clauses in the regulations, e.g., "appropriate data on rate of decline of residues on the treated crop," "such additional pertinent information as the Administrator may require," etc. Although it may require up to 2 years to obtain the experimental use permit, it does not follow that the registration and pesticide development process will be increased by the same time because much, if not all, of the data required for the permit may have to be obtained eventually for full registration. The extension of the R&D and registration process will probably result more from the administrative and processing delays rather than from the added data requirements. (As mentioned earlier, the costs will increase because of the need to obtain toxicological and environmental data in applications for experimental use permits for many potential products and not only those few potential products which have passed the field test program.) Industry's fear of delays and lengthening of the time frame stems from the indications in the regulations that at least 90 days will be required for review of the permit application. Also, past experience indicates that the timing of the experimental use permit is critical. A permit granted in September for product use on an insect pest which is prevalent in June or July is of little value to the developer since he must wait until the pest appears again. Industry almost always expects to lose "a growing season" because of the turnaround time in getting an experimental permit and in making the necessary arrangements for the field program. There should, however, be little additional delay because of this 90-day review requirement.

A more important change in R&D activities may be the shift in timing of parts of the process. The extensive toxicological, environmental degradation, residue and metabolism studies have in the past been done concurrently with, and sometimes after, extended field studies which frequently came under the permit system. Under the new regulations, as anticipated by industry, the initial work in these areas will be required before an experimental use permit is approved. Thus developers will have to make this initial investment earlier in the development process, and the risks associated with these earlier expenditures must be borne by industry.

f. Development of Market Data

A major benefit that the developers of pesticides receive from the previous experimental use permit system is marketing information derived from farmers, distributors and formulators as well as from the managers of their own field programs. Industry believes that the efficacy of the pesticide, the acceptance of the pesticide by farmers and distributors, and the advantages of the new pesticides compared to competitive products are best evaluated in the field program. They feel that the sale of the experimental product is beneficial, since it helps determine how much farmers and others may be willing to pay for the product if it is commercialized. (The actual cost of production of the pesticide at this stage is usually high, but developers can adjust the sales price to determine if they should plan to distribute the new pesticides.)

They also obtain reactions from the farmers and gain knowledge and experience with the product. The developers use the permit system to enable them to contact more farmers indirectly through the distributors and indirectly to obtain distributor loyalty. Marketing information is needed from several parts of the country in order to make decisions as to whether to continue to pursue a potential product, or to determine if they should make the necessary capital investments for new production facilities. Industry relies on these market data to distinguish between "the compound that looked interesting" and "the one that could really be made into a new product." Industry feels that the cost of the proposed experimental use permit as well as the restrictions imposed will limit the amount of marketing information that will be obtained in a practical sense, and thus hamper the decision-making process in pesticide development. This process could also result in a decrease in the number of new compounds brought to the marketplace in any year because of the hesitancy of industry to go ahead when a product performance or its acceptance is not as well known as it has been in the past.

g. Small Companies/Large Companies

It is the general concensus of industry that the proposed experimental use permit system will have more of an impact on the small pesticide companies than the larger companies. This is because the smaller companies presently rely more on the agricultural research services and state or federal facilities than large companies. Many of the smaller companies have only one experimental farm and cannot afford to enter into long-term leases for large test areas or purchase farms in several parts of the country. The smaller companies frequently rely on distributors or dealers to assist in the test program and feel this will not be possible with the proposed resale provisions of the regulations. Generally, the larger companies have several research farms or large leased areas in which they can test under the permit system. Further, they are more willing to make the large capital investments needed to keep up these properties for experimental use. Where possible, we expect large companies to use their own experimental farms for the field work necessary to obtain registration data.

h. Biological Controls

The discussion in the Federal Register preceding the proposed regulations on experimental permits suggests that special procedures or information requirements be provided for experimental permits on innovative pest control methods. Certainly those developers of biological controls would welcome changes to eliminate what they believe are unnecessary tests or inapplicable data requirements. Further, it is generally accepted that many biological control approaches need larger test areas than other pesticides. Those not developing biological controls are opposed to giving special consideration to any group of compounds. Since they feel little is known about biological controls, such approaches should be carefully examined. The most tenable solution is a careful review procedure by EPA staff experienced in biological control approaches to determine the extent of data required before a permit is given and to carefully set limits for the amount of material to be used, the acreage, the monitoring and reporting of results. (This same practice should be used with traditional pesticides as well.)

i. Other Impacts

A probable impact of the proposed regulations is the increase in the number of permit applications that EPA will receive, and a corresponding number of requests from the applicants to act on the applications as rapidly as possible. EPA should increase its staff with trained people to meet this demand. Since many permits are requested in the fall for experimental use in the spring, it may be possible to shift some of the EPA staff to meet the seasonal demands of the permit system.

j. Summary of Impacts

The field test portion of pesticide development is very important to the commercial developer. In addition to obtaining data required for registration on toxicity, environmental fate, etc., the developer requires field testing to obtain practical data on application rate, environmental and geographical effects, and most importantly to obtain a market reaction to the new proposed product. In the past such information was obtained from federal and state agencies including universities and colleges (who did not need a permit) and through direct contract with farmers or through distributors (often with a permit). These resources may not be as readily available to the developer as previously because of the restrictions of the proposed regulations (no resale, limited exemptions, etc.). Thus industry believes that experimental use permits will, in essence, be a mandatory part of the development process, and as a result cause increases in costs--more land for tests, increased data requirements for permit, destruction of crops, etc.--changes in timing--requirements for environmental data prior to permit, additional delays in obtaining permit--and increasing risks--lack of marketing data and performance data compared to competitive products. The proposed experimental use program will reduce any environmental impact of new pesticides and will provide for better control over the total experimental use of pesticides.

Most pesticide developers compare the experimental use permit process and resultant field studies to the "pilot plant" operation of a chemical industry. It provides an opportunity to determine the practical aspects of the pesticide, its use and application and to obtain other information which determines whether the product will be successful or not--range of cost, acceptance, etc. If this step is essential to the development of pesticides by commercial organizations, then sufficient flexibility should be added to the experimental use permit system to enable industry to obtain these data, given sufficient public health and environmental safeguards. For example, toxicity data is acknowledged by all as necessary. Data on environmental fate depends upon the chemical, its properties, the intended use, locations, area, etc., and may be necessary in certain circumstances. By carefully restricting the quantities which can be used and the acreage, control can be maintained over the environmental impact. By permitting resale, but still requiring data on use locations, participants, etc., a self-limiting process will occur on how many locations will be tried by the developer. A balance between costs of paper work and product purchases and information to be obtained will be achieved.

Limiting field testing may hide undesirable and unanticipated side effects until such time as the product is in wide distribution. The risks in the pesticide development process are sufficiently great that experimental use permits will probably be obtained by developers under the new system with as much cost as possible transferred to the ultimate consumer, including the cost of poor investments pursued by companies because of lack of data previously obtained under the old experimental permit system.

4. Restricted Use Pesticides/Certified Applicators

The restricted/general use classification system and the requirements for certified applicators have little or no direct impact on research and development activities, in the sense that they do not require additional data, research activities, expenditures of research funds, additional R&D staff, or change the time frame of research and development.

One of the major changes in FIFRA, as amended, is the classification of pesticides for general use, restricted use, or both. Section 3(c)(1)(F) indicates that the applicant for registration must request that the pesticide be classified for general or restricted use, or both. Under Section 3(D) the principle of classification system is explained. If the Administrator determines that the pesticide, when applied in accordance with the directions for use, or in accordance with widespread and generally accepted practice, will not generally cause unreasonable adverse effects on the environment, he will classify the pesticide, or the particular use of the pesticide, for general use. If he determines that similar use of a pesticide may generally cause, without additional regulatory restrictions, unreasonable adverse effects on the environment, including injury to the applicator, he shall classify the pesticide, or a particular use of the pesticide, for restricted use. If a pesticide is classified for restricted use because of acute dermal or inhalation toxicity, the pesticide shall be applied only by or under the supervision of a certified applicator. If the pesticide is classified for restricted use because it may cause unreasonable adverse effects on the environment, it shall be applied only by, or under the supervision of, a certified applicator or may be subject to other restrictions by regulation. Change in classification may be made by the Administrator; appeals to any change, as well as original regulations on restricted use, are provided for. Section 4 provides that the Administrator shall prescribe standards for certification of applicators of pesticides, provides for both federal and state certification, and for state plans for certification. Regulations for the classifications of new pesticides shall be promulgated by

October 1974; all previously registered pesticides shall be reclassified between October 1974 and October 1976; requirements that a pesticide be registered for use only by a certified applicator are not effective until October 1976, and certification of applicators will occur in the four-year period up to October 1976.

Previous to FEPCA, classification of pesticides and requirements for certified applicators were non-existent, although many states had programs for licensing pest control operators.

Although the classification system and use of certified applicators are separate entities in the law and in the regulations to be promulgated, they must be combined in considering any possible impact on research and development activities within the pesticide industry. The classification system has not yet been adopted by EPA, and industry has some concern and uncertainty over how the law will be implemented. As a result, the possible impacts of implementation of this part of FEPCA are uncertain. The following discussion describes industry's anticipation of how the regulations will evolve, presents some of the problems anticipated, and summarizes the principal impacts of the restricted use/certified applicator provisions on R&D activities. Implementation of this part of the law will have more significant effects on the marketing of pesticides than direct effects on the R&D process.

a. Anticipation of the Restricted Use/Certified Applicator Program

The law specifically provides for designation of restricted use on the basis of toxicity or hazard to the applicator or other persons, or on the basis of unreasonable adverse environmental impact. Industry generally believes that the restricted use designation on the basis of toxicity, inhalation or dermal, is reasonable, is justified, and is important to protect the applicator. Further, industry believes that toxicity will be the principal determinant of the classification, when a final classification system is adopted. Industry fears that in some cases, restricted use will be designated only because of environmental grounds, e.g., as a result of persistence, although there is acknowledgment that some environmental effects, such as biomagnification, may be valid cause for restriction. This could lead to differentiation among products in the registration process with little concern for efficacy, but placing the importance on environmental effects.

Industry anticipates that a sizable number of compounds will be classified for restricted use. (Some companies we contacted indicated that they expect all of their important pesticides for major crop use would be classified restricted; others, however, felt that they were working primarily on "safer" pesticides and expected most of them will be in the general use category.) In either case, there was no great concern over the number of pesticides classified as restricted, as long as the criteria for evaluation are consistent. Large companies, with a broad product line were, in general, less concerned than smaller companies. Serious objections were raised by many companies on the plans to designate a pesticide as restricted use for all its applications, as opposed to treating each use on a case by case basis. It was strongly felt that the method of application, type of applicator, acreage covered, etc., should play a part in the designation of the classification, rather than the chemistry alone.

Industry anticipates that there will be a large number of certified applicators after the initial period of standard setting and submission and approval of state plans. Industry feels that "practically every major farmer" or "most farmers" will be able to "pay their $2 and be certified." Industry's general view is that the farmer is becoming more and more intelligent about the use of pesticides. As long as the tests for certification are practically oriented and are not based only upon written theoretical questions, many farmers should be certified. Industry feels that if there are many restricted use pesticides, there will have to be sufficient certified applicators or the whole program will be inoperable. Most likely political pressure in agricultural states will result in a sizable number of certified applicators.

Industry was uncertain as to whether the designation of restricted use (with concurrent safety for the applicator and environmental protection) would allow specific pesticides to be registered more easily than without the designation, e.g., allowing registration of a particularly toxic material for a specific important use, because the applicator and environmental safety was assured. About half felt that this was a reasonable possibility, the remainder thought it was possible only in theory or did not feel that this was the intent of the regulations or would be practical.

b. Problems and Benefits from Implementation

Some of the problems envisioned in the development and implementation of the law with regard to restricted use and certified applicators include:

- Achieving a reasonable balance in the classification system between environmental and safety criteria for the restricted use designation.

- Finding a sufficient number of certified applicators in the country, if high standards are set for certification.

- Assuring that the state programs for certification are adequately organized and implemented, i.e., sufficient competent state staff, model state regulations, elimination of cross licensing requirements for dealers and distributors.

- Providing help to the small farmer, who because of size and acreage, is unable to obtain services of certified applicator and may not wish to or be able to be certified himself.

- Assuring that the "home and garden" oriented formulations are not affected significantly.

Most of these problems will be solved by reasonable implementation of regulations by the EPA and cooperation and coordination with the states.

In addition to the obvious benefits of implementation of the regulations on applicator (and other persons) safety and protection against adverse environmental effects, several companies felt that the use of certified applicator would prevent or at least restrict the tendency of many pesticide users to "overkill" in the application of products. Others felt that the increased "importance" and "availability" of the certified applicators could lead to good ecological effects, lower overall use of pesticides and encourage scouting programs and improvements in integrated pest management. Others felt that a benefit, or at least a beneficial impact, would be the enhanced growth of a "total service concept" in which an organization provides the farmer with all of the required pesticide services, from seed treatment, through various applications of insecticides, herbicides, etc., with a guaranteed yield in return for a portion of the profit. Staff of organizations offering the concept would be certified and trained in the use of pesticides. Such a concept may help establish an optimum use of pesticide.

c. Impacts on Research and Development

We found that the general concensus among industry was that there would be no direct or immediate effects of the restricted use classification or certified application program on the principal research and development activities in the pesticide industry. Secondary effects, resulting from decreases in potential markets for certain compounds, or uses, could influence the research decision-making process, and thus change some of the direction of the research effort.

Industry feels that major purchasers will not greatly prefer the general use product over the restricted use product because the user most likely will be a certified applicator, and the more toxic compound classified as restricted use will most likely be more effective and may be less costly.

In the R&D process there will always be some uncertainty as to whether a specific pesticide will be classified as restricted or general upon registration. If environmental factors become important classification criteria, it will be difficult to determine early in the R&D stages which classification will result because many environmental tests are not conducted until extended field studies. Thus the research must continue if the product has promise of effectiveness and competitiveness. Given two equally effective products for the same market in the early stages of the research process, one of which would most likely be ultimately classified for restricted use, and the other for general use, industry would normally continue to develop both products until production cost and marketing cost information are obtained. If the general use product had an anticipated equal or only slightly higher production and sales cost than that anticipated for the restricted use product, the general use product would be pursued at the expense of the other. If the restricted use product had a lower production and sales cost, industry would not shy away from its development because of its anticipated classification or certified applicator requirements. This decision may be tempered by the number of certified applicators and the type of testing required to be certified--if the number is sufficient, it will not affect the decision to pursue the restricted use product.

In general, industry feels that given sufficient time and money, it can get almost any good effective product registered. Only if the restricted use category severely affects the market of the possible product, and this must be determined on a case by case basis, will research directions be changed and greater emphasis placed on seeking the general use product. (There is some belief that the restricted use categorization could benefit marketing because sales will be limited to only certified applicators and not to the public, thus reducing the number of sales contacts and costs incurred.) Some effort in the R&D process can be anticipated to determine the probable classification of candidate products, once criteria have been formalized and adopted.

Concerning minor crops and pesticides registered for minor uses, the general conclusion is that there are so many factors preventing the development and registration of these products, that the restricted use category would not severely affect marketing of the product. Industry is generally unwilling to develop these products, and there may not be sufficient available products in the future, so that any additional expense or difficulty of the certified applicator will probably be borne by the user and passed to the consumer. For uses such as right of way brush control, where the users are limited but well defined, industry feels the restricted use category will have no effect. There may be some problems in companies that emphasize home and garden products, if these are classified as restricted.

Another area of concern, and possible impact, is the reregistration and classification of existing products. If industry feels that a restricted use classification could lessen the market share of an existing product, perhaps because of the existence of a similar general use product, it may not make the investments required to reregister the product when the current registration expires. This will most likely affect minor crops and products used on those crops.

5. Section 3(c)(1)(D)

Originally strongly supported and now only partially supported by industry, this section of FIFRA, as amended, will probably provide administrative and procedural problems for both EPA and industry but will have little impact on research and development activities.

Section 3(c)(1)(D) of FIFRA, as amended, requires that, "if requested by the Administrator, a full description of the tests made and results thereof upon which the claims are based, except that the data submitted in support of an application shall not, without permission of the applicant, be considered by the Administrator in support of any other application for registration unless such other applicant shall first have offered to pay reasonable compensation for producing test data to be relied upon and such data is not protected from disclosure by Section 10(b)." The law then establishes the method for determination of payment and terms or conditions with appeal procedures.

Prior to FEPCA, the Administrator was not constrained from using data provided by other registration applicants, and no payments for data use were required, unless it was privately arranged among the applicants. The data submitted, to our knowledge, was held confidential with the USDA, FDA, and EPA. However, this procedure permitted the registration of products by "me too" applicants, those who did not incur much of the costs of the development process, but could capitalize on earlier registration of a pesticide by others when the patent provisions had expired. Industry strongly supported in the inclusion of Section 3(c)(1)(D) in the law "to foster research and development of new pesticides by assuring a degree of protection for the developer in procuring the efficacy and environmental effects data submitted to the Administrator to secure registration of a new pesticide."

In November 1973, EPA issued a policy statement clarifying and implementing a portion of this section. The policy indicated that all applications for registration (new, amendments or renewals) must have an express offer to pay reasonable compensation for use of test data submitted to EPA with a registration application for the first time after October 21, 1972. Further, it provided three categories for registration application--2(a) where all supporting data was provided in the current application; 2(b) where references to all data were provided (from open literature or past applications); 2(c) where registration was sought under use patterns, efficacy and safety previously established, i.e., use of other applicant's previous data although additional new data could also be provided. The policy also called for publication of the name of product and active ingredients in the Federal Register for each application, and for the availability of the labeling furnished by the applicant. A procedure was specified for anyone who desires to claim subsequent compensation under 3(c)(1)(D) to file notice with the Administrator, and procedures for proceeding with the applications under 2(a), (b), or (c) were prescribed. The issue of determination of appropriate and reasonable costs for compensation for data was deferred until additional regulations could be promulgated.

Clearly the intent of the law was to provide some degree of equitableness to organizations that had borne the costs of a portion of the research and development activities required by pesticide registration. In some respects, this section is viewed by industry as an alternate method of prolonging the proprietary life of a pesticide. One of industry's concerns was the "me too" registrants, who, under FIFRA, could produce, market and register a product having ingredients on which patent rights had expired, with little expense, if any, to achieve registration. As the registration process became "longer" under FIFRA, and the available patent protection period shorter, the number of good marketing years for "me too" companies became greater and the industry that sustained the R&D efforts could lose part of their market. Thus 3(c)(1)(D) was looked upon as very beneficial to those who conducted R&D on pesticides.

Our discussions with industry provided a large number of complaints and opinions on the proposed implementation of 3(c)(1)(D); but, in general, very few significant impacts on the R&D process could be ascertained. Some of the principal objections to the proposed implementation of 3(c)(1)(D) were:

- Time of Implementation--Only data submitted to EPA in a registration for the first time after October 21, 1972 is considered for compensation. Industry feels that the cut off date should be extended back into FIFRA. Perhaps the reason is that many of the products in recent "me too" registration applications have recently had patents expire--the original registration for these products must have been submitted long ago. Second, many larger companies feel that there were many "me too" registrations between October 1972 and November 1973 because a policy was not established.

- Administration Delays and Paperwork--Many companies we contacted complained about problems in paperwork, i.e., submittal under 2(a), (b), or (c) and having their applications returned with requests to submit under another category. The 60-day period before processing under 2(c) also drew criticism. These reactions are probably due to implementation of a new system and can hardly be thought of as adding significant delays to the registration process or impact to R&D.

- Publication and Availability of Information--There was some concern over publication of information in the Federal Register of each application; however, all recognize that companies must some way be made aware of those who would like to use others' data. There was some concern about the availability of labeling information. In general, there needs to be a clarification of what is considered as proprietary or "trade secrets" under section 10 of the law, and what information is considered "for compensation" under 3(c)(1)(D). Industry believes that some efficacy and application data appearing in the label is a "trade secret" at the time of registration. Clearly, once a product is registered and marketed, its label is no longer a trade secret. A principal objection is that availability of such a label can give some information to a potential competitor a year or more before final registration and could be important in a competitor's development program. Also, there is considerable confusion as to the information that is publicly available under the Freedom of Information Act as compared to Section 3(c)(1)(D) under FEPCA. It may be that 3(c)(1)(D) is under criticism for unjust reasons.

- Interference with Intercompany Arrangements--Some organizations believe that 3(c)(1)(D) is unnecessary because it interfers with licensing and agreements to manufacture, distribute, etc., which exist among companies. In any case, there is probably little affect on any R&D activities of these companies since they can now and should be able to continue to agree on reasonable compensation with or without the EPA procedure.

- Establishing Appropriate Compensation--Although detailed procedures for establishing appropriate compensation have not been proposed, many feel that the compensation issue will have to be resolved in court soon. The general consensus of the larger companies is that the compensation will be too low; yet several do not want a case brought to court now to set precedents for the future. All agree that if a reasonable compensation is provided for, the industry and the public will benefit from 3(c)(1)(D). Of course, one's definition of reasonable depends upon whether one is the buyer or the seller.

- Other Impacts--Several industrial representatives felt that an effect of 3(c)(1)(D) was to prevent publication in the open literature of recent data on pesticides. They felt that this would impede hiring of good research staff who felt the need to publish. Although we agree that, prior to registration, there is little incentive to publish, afterward there is every reason and we believe this issue has little impact on R&D effort.

In the long term, implementation of 3(c)(1)(D) will be marginally beneficial to industry's R&D efforts. After the initial administrative procedures have been fully developed, some reasonable values have been set for the data to be used in registration, and clarification of trade secrets and compensatable data is made, the intent of the law will be achieved. The impact on R&D activities will, in general, be small. Unless the value set on the compensatable data is higher than industry now estimates, the amount will be small compared to the total development cost of the pesticide. Companies are probably not going to conduct additional R&D in the hope that they will be compensated when someone else uses the data for registration of a product.

Sufficient process work, product development, and marketing efforts will generally have been undertaken so that the "me too" registrant cannot easily catch up without some expenditure. The cost of the compensatable registration data will probably be small compared to the "me too" company's production and marketing costs if the company is to obtain significant market penetration. Elimination of the "me too" companies by setting too high a value on data is not in the best interest of the public. The general consensus is that economic conditions and the free enterprise system will eventually have much more impact on R&D efforts (and pesticide production practices) than the 3(c)(1)(D) implementation.

6. Reregistration of Existing Pesticides

The reregistration of currently registered pesticides in accordance with the new provisions of FEPCA most likely will increase non-innovative research and development activities by industry for a two- to five-year period and will catalyze the removal of present marginally profitable pesticides, particularly those for minor crop use, from the market. Industry has given little attention to reregistration to date because of other more pressing issues associated with FEPCA implementation.

FEPCA, under Section 6, calls for cancellation of the registration of a pesticide after a five-year period from original registration, unless a request is received from the registrant, or other person with the concurrence of the registrant, for continuation of the registration. Publication of intent to cancel will be made in the Federal Register. This is essentially the same provision as that given in Title 7, Ch. III, 362.10 (i) of the Regulations for the Enforcement of FIFRA, with the exception of the publication of intent to cancel.

A more important part of FEPCA, with respect to reregistration, may be the section describing the effective dates of the provisions of Section 4, Registration. The law indicates that "after two years, but within four years after enactment of this Act, the Administrator shall register and reclassify pesticides registered under the provisions of FIFRA prior to the effective date of regulations promulgated under Section (c)(1) [October 1974]."

There is some concern as to whether the above requirement means that all previously registered pesticides will require reregistration (with appropriate pesticide classification) within that 2-year period, or whether only the classification of restricted use or general use will be made. The general belief is that only reclassification will occur and that reregistration will be required only at the end of the normal 5-year period. However, additional data may be requested by the EPA to support the reclassification procedure. Much of industry is adopting a "wait and see" attitude toward registration, or are doing very little towards this goal, except as their current registrations expire, because they are uncertain of the procedures to be followed.

We believe that each currently registered pesticide will be carefully examined by its registrant when reregistration is required (after the guidelines for registration and restricted use classifications are issued). If the product is (1) marginally profitable, (2) has a relatively small volume, (3) is expected to be classified for restricted use, (4) will require considerable new data on toxicology, environmental degradation, or environmental effects, or (5) has little or no patent coverage, the tendency will be for its developer not to request reregistration. We were given examples of specific products by several companies that would not be reregistered, because the cost of obtaining the added data would be greater than the reasonable projected income over the next few years. Most companies feel that the greatest additional data requirements will be in environmental effects. For most of these compounds, there were only small markets, mainly on minor crops. Some narrow spectrum pesticides will also not be reregistered; this would be counter to the emphasis of EPA.

The number of pesticides that will not be reregistered will depend primarily upon how much additional data is required and the market size. A product which was originally registered in 1970, after PR 70-15, may need only modest additional data, and thus if a reasonable market exists, the necessary reregistration effort will be expended. Estimates of the additional effort required for reregistration range from 0.5 to 6 man years per product. One problem expressed by several groups was the extension of time for reregistration; for example, if additional 2-year carcinogenesis studies and other long-term studies were required.

This reregistration effort will to some degree detract from innovative research and development activities; it will require more analytical chemistry, field testing and additional regulatory support efforts. With a limited number of staff, effort will be withdrawn from the search for new products or innovative activities, which may have more risk than the reregistration of an existing marketable compound. Each compound will require its own cost/benefit analysis for specific products in making these decisions. Simply stated by one organization, "if the product is hot, it must be reregistered; if not, we will forget it."

It must also be remembered that there is a natural attrition of pesticides as they outlive their marketability and as they are replaced by other more effective, less costly, or more profitable products. This causes industry not to reregister certain products as a general business decision. Since data requirements under the new law have not changed drastically, we cannot expect drastic changes in current practices of industry in dropping products when they are no longer useful and profitable. However, the emphasis on environmental effects in FEPCA and the registration uncertainty will probably increase the number of product dropouts. This will have the beneficial effects of an overall reduction in potential adverse environmental effects, and in the long-term provide more incentive for industry to give greater emphasis for the environment in its pesticide development process, but at the expense of neglecting means to protect small volume crops.

7. Other Specific Impacts of FIFRA, as Amended

Table 9 in Section IV B indicated a number of other changes as a result of passage of FEPCA and the regulations promulgated or proposed to date. From our discussions with industry, we believe that most of these changes will have only minor impacts on the research and development activities in the pesticide industry at the present. There may be specific problems for industry created by these portions of the law and the regulations, which could result in an increase in cost or increase in effort in pesticide production. However, there will be little, if any, impact on R&D activities. Some of the principal comments of industry and any related impacts of these portions of the law are briefly discussed below.

a. Indemnification

Section 15 provides for indemnity payments to persons who owned a pesticide, the registration of which was suspended or cancelled because of actions necessary to prevent imminent hazards, and who suffered losses by reason of the suspension or cancellation. At the beginning of our study we hypothesized several possible effects could occur: (1) EPA could be more cautious in granting registration because of the possibility of indemnification and required payments; (2) once registration had been granted, EPA would be cautious about suspension or cancellation to avoid indemnification; (3) industry would feel that this clause reduces some of the risk in pesticide development and as a result would be willing to try more innovative approaches with certain potential pesticides. From our discussions with industry, and limited discussions with EPA staff, we conclude that none of these original hypotheses are valid. Industry, in general, feels the indemnification section will have no effects at all on the pesticide R&D process. The general consensus is that new chemicals are always given a cautious and extensive review, indemnification will not make the review more cautious or thorough. Second, industry believes that if any valid safety or environmental reasons are found to suspend or cancel a registered pesticide, EPA will exercise its authority (and obligation) without consideration of indemnity. Third, industry doubts it will ever recoup significant losses through the indemnity clause. The risk in pesticide development is not reduced, and with the current review process, industry doubts if any new registered pesticides will be recalled or suspended quickly. Several industrial contacts considered that this section "opened a can of worms," but did not believe there were strong impacts on R&D.

b. Books and Records/Registration of Establishments

In general the provisions of the books and records sections of FEPCA are very similar to those of FIFRA. Industry expects greater inspection and enforcement of these books and records, and as a result may incur some extra effort and expenditure in assuring their completeness and availability. However, the information required is generally available from company records and the impact of the law is felt by industry to be only another "administrative headache." The books and records section may add some work to formulators and those who prepare chemicals on a contract basis. No effect on research and development is anticipated.

Registration of pesticide establishments also will provide little impact on research and development activities. Administrative effort and expense will be required to assure that labeling is correct, to account for the large number of manufacturing facilities any one company may have, etc.

c. Packaging and Disposal

FEPCA provides that the Administrator shall establish procedures and regulations for disposal and storage of packages and containers of pesticides and excess amounts of pesticides. Industry, in general, is concerned about the problem of disposal of packages and containers, and pesticides themselves. The impact of the regulation is unknown. Various segments of industry have been working on the problem. Some large companies conduct their own packaging research, some of which is on "disposable" or "degradable" packages. Others support the efforts of NACA in this area. The research and development activity in packaging and disposal is at the moment modest. There is some concern for "child proofing," the development of disposal sites for pesticides, economic approaches to recovery of pesticide containers, etc., and the general feeling that "some day there will be a significant container disposal problem." Industry feels that this "low level" of research and development activity will continue but that FEPCA will have little overall impact. In general, they are more concerned with disposal problems under the effluent guidelines regulations and ultimately under the provisions of the Hazardous Waste Management Act.

d. Unlawful Acts, Enforcement, and Penalties

As mentioned earlier, the series of unlawful acts, methods of enforcement, and penalties involved in FEPCA are all "stronger" than in FIFRA. These provisions, by themselves, do not change the research and development activities of the industry. Industry expects greater enforcement, receipt of severe penalties for violations, and careful scrutiny by EPA (both the OPP and through regional offices). They expect as a result that they will have to be cautious and careful in all of their operations, particularly those involving administrative actions, records, shipment, inspections, permits and labeling. They believe that they are very careful and cautious now in actions dealing with safety, environmental effects, data reporting, etc., since it has always been in their best interests, and as a result no significant impacts of the new law will result. Some of the larger companies felt that the increased costs of the entire pesticide operations as a result of any additional caution, records keeping, etc., to avoid penalties, would also discourage the continued efforts in pesticide for minor crop applications. Further, they felt that whereas the major producers could afford the occasional mistake, leading to a penalty, the smaller companies could not. This would make the operation of small companies more risky, and ultimately reduce the number of marginal or minor companies in the field.

e. Intrastate Coverage

FEPCA also regulates pesticides produced and used, entirely within a single state. The nature of the industry--a limited number of establishments conducting research and development, most of which sell and ship pesticides to several states (and internationally)--is such that little impact, if any, on R&D activities will result from the addition of intrastate coverage. There may be some significant changes in the total activities of formulators and distributors because of FEPCA but these elements do not contribute significantly to the R&D output of the pesticide industry.

f. States Authority

Under FEPCA state authority has both been partially extended and restricted. States can regulate the sale or use of pesticides, but not in contradiction with sale or use prohibited by EPA; states cannot require additional labeling or packaging requirements; states can provide registration for pesticides to meet local needs if the state is certified by the Administrator, and if registration for such a pesticide has not been denied, cancelled or disapproved by the Administrator.

The impact of these state authorities on research and development is probably small. However, there is some general concern that some states may not be able to handle the requirements for registration to meet local needs. Most likely these states will not be certified by the Administrator to register "local use" pesticides. Thus the agriculture and other industries in these states may be deprived of some pesticides. Industry would like help from EPA in providing guidance and support to these states. Another concern is for more coordination generally between the states and EPA to assure that the standards for applicators to be certified and experimental permits to be issued by states, are uniformly imposed by the states. Generally, industry expects a number of state problems in disposal, certified applicators, etc., but feels that little impact on R&D will occur.

D. GENERAL IMPACTS OF LEGISLATIVE AND REGULATORY ACTIONS--RELATIONSHIP WITH OTHER TRENDS

In the previous section we have described the specific impacts of the various sections of FEPCA on research and development activities in the pesticide industry. These impacts are interactive, and some broad changes and trends in the pesticide R&D process can be anticipated as a result of their combination. Furthermore, there are general trends in the industry related to economic considerations, the energy crisis, shortage of raw materials, increasing labor costs, political and public pressure to increase agricultural production, etc., which also produce trends and changes in the research and development process for pesticides, particularly when combined with the impact of legislative actions. In this section, we will present some of the general impacts and changes anticipated in the industry, including a discussion of how the trends described in Section III relate to R&D. Then we will briefly describe some of the more important benefits to the public and to industry of the implementation of the current law.

1. Research and Development Costs and the Direction of Research Effort

As illustrated in Section III, the costs of the various portions of the research and development process has been increasing as a result of additional data requirements, extension of the time frame, and other regulatory activities. In general, synthesis costs have not increased significantly beyond the normal inflationary increases for all R&D activities. The cost of primary and secondary screening of pesticides, activities conducted generally in the laboratory, has also not increased greatly. Significant increases have occurred in the field test portion of pesticide research and development, in the laboratory and field work required for development of safety and environmental data (residue, toxicity, metabolism, environmental fate, etc.), and in the administrative efforts required to achieve registration. Of course, all costs have increased due to inflation over the last few years. The question to be discussed here is: what is the feedback or resultant effect on the pesticide R&D process as a result of increasing costs of the various segments of the process?

Considering first the overall economics of a pesticide industry, the percent of product sales devoted to research and development is relatively constant or at best has been increasing slowly. The percentage of sales devoted to R&D depends greatly on the individual company. In general, the quantity is several times higher than traditional of the basic chemical industries, but not as much as that spent by the pharmaceutical industry. Values of 4 to 8 percent of sales are typical. Sales of pesticides have also been increasing over the last years, although there has been a considerable decline in sales of older, harder pesticides, such as the chlorinated hydrocarbons. The greatest increase in pesticide sales has come in the area of herbicides, particularly new herbicides for use with major crops. Thus, the total number of dollars available for research has been increasing roughly in proportion to sales.

The net effect of these factors, combined with current economic trends in the agricultural chemical industry, is a change in the balance of research effort to increase efforts which bring short-term return on the R&D investment, and to reduce the effort which can bring long-term, but relatively uncertain, return. Specifically, there is a greater emphasis in most companies to capitalize on existing products. Research emphasis is placed upon conducting the required "defensive research" to maintain the registration of products for existing uses. Maintaining the registration of a proprietary, patented product which is sold competitively in the marketplace, takes priority because it is the least risk road to profitability. Research emphasis is also placed on those studies required to add new crop uses to existing products, provided there is sufficient market. As a corollary to this emphasis, there has been a general decrease in funds available for long-term research and development investments, thus this longer range R&D must be more selective. Several companies have dropped research in areas of marginal sales or profitability, i.e., fungicides, nematocides, certain insecticides, etc., and minor uses. Second, emphasis on new, innovative approaches to pesticides has been reduced since this investment has even more risk than investment on conventional pesticides. Finally, long-term research investments have concentrated on the major agricultural markets at the expense of minor crops, right of way, home and garden supplies, etc. This change in balance between short-term research for short-term return and research for a longer term return varies with a specific company. Smaller companies which are more dependent on the profit from the sale of a limited number of compounds must emphasize the short-term return and thereby devote most of their work to maintaining and adding product uses to their currently marketable products. This may be somewhat shortsighted since it does not place them in a good competitive position for continuing in the marketplace 10 years in the future. The larger pesticides companies, on the other hand, and particularly those with sufficient capital resources, either as a result of major agricultural products or parent companies with a large base of industrial operations, can afford to continue their relatively high level of commitment to longer term research efforts.

In parallel with shift in emphasis, another trend, supported by the data given in Section III, is that the number of compounds which are developed and reached the marketplace is decreasing. As a result a greater number of compounds are permanently placed on the shelf at sometime during the screening and evaluation process. The screening and decision-making process must become more effective in that approximately the same number of compounds or perhaps even an increased number are entering the screening process. Factors that can ultimately effect the decision to go ahead with a particular product are, however, being used in the screening process at earlier decision points. For example, more effort may be placed on developing better estimates of production costs of pesticides, in order to make a determination of possible product competitiveness early in the process. As environmental concerns increase and if the trends in pesticide registration show that "environmentally safe" pesticides ultimately will be registered more easily than others, effort in environmental research will be needed to provide an early input to the decision-making process. There will also probably be a change in the synthesis approach to be more selective--use the "rifle shot" approach to pick chemicals for initial screening rather than the "shotgun" approach.

The end result is an increase in the number of possible pesticides which are "on the shelf." These are primarily chemicals with low efficacy, high production costs--chemicals which would never become commercialized because of economic or other reasons. The classification provisions and certified applicator system implemented by current law and regulations could help get some of these compounds off the shelf and into the market for special needs because more toxic compounds may be registered. Nevertheless, it will be increasingly difficult to find compounds that are comparatively better than those already on the market.

Another way of expressing some of the changes resulting from the increased cost of the pesticide R&D process is that the threshold for developing a winning pesticide has changed. The R&D dollar expenditures to develop this winner have increased, both for the specific product and for the product considering a number of other potential products which have been discarded. The market threshold for deciding to go ahead with any particular product, must necessarily also increase since the percent of sales devoted to research and development has been maintained about constant.

From a management viewpoint, there is little incentive to devote research and development dollars to innovative pesticide efforts with a high risk of long-term development, i.e., little or no return for at least seven to 10 years (the time for registration and initial marketing) when a short-term gain can be obtained by extending the use of a particular, already developed product to other crops.

Another impact of the increased cost of the R&D effort is for companies to seek an international market early to bear some of the costs of registration in the United States. A portion of the research effort is also being done internationally by the larger pesticide companies with only the necessary field tests and evaluation done in the U.S. The importance of the international market is increasing in the decision-making process.

The following changes in research direction occur:

- There is generally no change in the number of compounds synthesized and placed through the primary screen.
- Emphasis in the synthesis and screening process is placed on analogs and homologs of existing or already registered products rather than diversification into new or innovative types of pesticides.
- To some extent less effective compounds are pursued if they show great promise of safety and environmental acceptance and can replace existing more hazardous products.

- Efforts to simplify and streamline the screening process in terms of new instrumentation and better techniques are continuing.

- Emphasis is placed on development of analytical techniques and refined, but cost effective, methods of conducting environmental tests, residue analysis, metabolism studies, degradation studies.

- Research which is not in the "main stream" of pesticide development is done more and more under contract to research organizations, e.g., toxicology, carcinogenesis, toxicity to fish and wildlife, etc.

- There is a reduced emphasis on long-term programs in areas outside the traditional chemical pest control.

- Management demands more extensive and accurate data to support the cost benefit analysis in the decision to go ahead with a compound. This involves a more thorough examination of toxicology, environmental effects, as well as the process development itself.

2. Timing of the Research Process

There are three principal impacts of regulatory actions on the timing of the research and development process in the research and development industry: (1) an overall extension of the R&D process, with most significant impact on field studies and on data development for registration; (2) a re-ordering of parts of the research and development process with some changes in importance of the elements to the decision-making process, (3) iteration of portions of the R&D process brought about by EPA data requests and the need for better decision-making. Evidence for the overall increase and timing of R&D process and some of the reasons for the increases have been given in Chapter III. Over the past 15 years there has been a relatively continuous increase in the time period from synthesis or initial screening through registration of from 4 to 7 years over the period from 1960 to present. As mentioned earlier, some of the reasons for these increases in the overall time span have been the requirements for additional data--toxicological, environmental impact, residue, metabolism, runoff studies, carcinogenicity, teratogenicity, etc.--the delays in processing of information within the EPA and delays in reviewing requests for experimental permits and registrations. Other factors include the increased importance on obtaining reliable data for the decision-making process, the difficulty and need to obtain reliable market data for decision-making. In terms of re-ordering portions of the R&D process, toxicological work has now been moved up so that more extensive work is conducted earlier in the R&D process. Similarly the requirements for part of the two-year tests for carcinogenicity, etc., being necessary for the experimental permit, make it important that these tests be started fairly early in the process. Industry anticipates that a similar moving up of environmental studies may eventually occur so that some more environmental work is done prior to extended field studies than presently practiced. Similarly, there is a greater amount of earlier effort in analysis of the potential production processes and preliminary engineering design to access the costs of potential products. Some companies that have been willing to expend a heavier rate of resources early in the process have actually been able to decrease the process duration. However, most companies cannot exert this additional effort and their resources get divided among the efforts which are necessary at this early stage.

Most of the re-ordering of the research efforts is done in an attempt to make the decision-making process more effective and more accurate. If more effort is required earlier in the R&D cycle where a greater number of compounds have not yet been eliminated from the development pipeline, the overall costs of research increase as explained earlier. Thus there is conscientious effort to reduce the number of compounds at any stage in the process through focus on important decision points and more continuous review to eliminate products at the earliest possible stage. Thus the re-ordering of the R&D process can lead to increased efficiency in the R&D process.

The re-ordering of the R&D process also impacts the decision to invest in new production facilities. In the past such decisions were often made so that the granting of registration would correspond closely with the completion of plant construction and product availability for the market. This was true for both pilot facilities to produce pesticides for experimental use as well as for full-scale production facilities for general sale. Because of delays in registration encountered by several in industry and because of the desire of management not to commit large amounts of money for construction until the risks have been reduced as much as possible, the decisions for plant construction are now made closer to the end of the registration process than previously. The increases in the time required for plant construction and startup (not due to regulatory actions in general) further extends the time from which the product was first developed to when production in reasonable quantities can be achieved. The timing of the decision for plant construction process depends on the individual company, whether there are alternative facilities for manufacturing the pesticides, whether the intermediates are purchased from other companies, whether the raw materials must be purchased or are available within the company, and many other factors. Additional delays in getting production facilities on stream near the time of registration cannot be attributed to changes in pesticides regulations; in fact, the major influences on these delays are general economic constraints.

Lengthening the overall R&D process and re-ordering of priorities and procedures within the R&D activities have caused a secondary problem in terms of decision-making. The R&D process for most pesticidal chemicals has become close to the "half life" of a manager of the R&D process operations. As a result it becomes more difficult for a manager to see the product through from beginning (synthesis) to end (registration). This results in lack of association of specific people with specific products and less motivation or inspiration for continued development effort. The extended duration makes the development process "a little less exciting," and leads to a decrease in motivation of all the participants.

Another impact of timing relates to iteration in the R&D process as it now is conducted. Requests for additional data from the EPA, changes in data requirements and guidelines, or changes in regulations may occur during the development process of a product (for example the PR 70-15 change, a change from FIFRA to FEPCA, all of which would occur during the development process of a pesticide first synthesized in the period from about 1967 through 1970). As a result, work in several different segments of the R&D process is never completed but left open-ended for continued effort at a later date. Toxicology studies may be performed over several years time, with concentration of efforts at various points, whereas in the past it may have been done at one time by a group of individuals working on a particular chemical. To some extent this reiteration process can lead to inefficiency, lack of motivation or incentive, and lack of productivity.

3. Staffing of R&D Activities

Although the impacts of legislative and regulatory changes on the R&D staff of a specific pesticide company depend greatly on its size and type, some general conclusions can be drawn. The R&D staff of the pesticide companies who conduct innovative research and development has increased. The number of biologists, environmental chemists and engineers in particular have increased. Also the number of people involved in regulatory liaison, and in patent and legal departments, have increased. The field test staff has remained about the same, although significant changes are anticipated as a result of the proposed experimental permit regulations. Some interchange or substitution of staff from one job to another has occurred. It has generally not been possible to use the synthesis chemist in work requiring environmental biology, entomology, or in regulatory liaison. However, chemists with a strong analytical background can participate in environmental chemistry, residue studies, etc., areas which have seen a large increase in labor requirements to meet the data requirements of registration.

There is a reasonable amount of mobility among the staff in pesticide companies. In our discussions with industry, we found that frequently a manager or researcher with one company gained experience at another company. People who leave major companies because of a cutback of a particular phase or area of the research program often find similar jobs in the same specialty in other companies. Companies vary somewhat in their staffing policy; smaller companies and some larger promote the "family" feeling--provide long-term security for its employees and promote from within as in many other chemical industries. R&D staffing in the pesticide industry is probably not significantly different than in most chemical or pharmaceutical companies.

Another effect of the regulatory process on R&D staffing is for companies to focus in certain market (and R&D) areas, i.e., herbicides, insecticides, etc., and to build centers of expertise in these areas. Specialization has also occurred through the more extensive use of outside contractor support in the pesticide R&D process. Several companies subcontract their toxicology efforts, some environmental biology, analytical chemistry, or fish and wildlife studies, to other laboratories. A few companies have gone even further by having their screening done on a contract basis; others are beginning to have their field test work done by contractors. Frequently this specialization results from a desire to reduce the costs of the pesticide R&D process and to focus on those portions which are more critical to the pesticide development process, rather than those which fit only into specific registration requirements.

There is considerable diversity of opinion among industry as to where new R&D staff should be added. Many larger companies would prefer to see new staff added to promote innovative research and the development of new products, primarily new chemicals. Other companies would prefer to see staff added to development efforts associated with additional registrations of existing compounds on other crops. The greatest increases in staffing in most companies have occurred in "defensive research" and in "field development studies" so that registrations can be maintained and new products added to the registration.

In summary, we expect a slow but relatively steady growth in R&D staff within the industry, partially due to legislative changes, with concentration on analytical chemistry and environmental science.

4. Patents

As part of this study, we attempted to assess the significance of patents and patent protection to the R&D activities in the pesticide industry. Very mixed reactions were obtained in our discussions with industry on the importance of patents. Most companies concluded that as a result of the extension of time required for pesticide registration, the remaining useful patent life of most pesticides is about 10 years. Practically all companies would like to extend this patent life through issuance of the patent at the time of registration or through a patent system such as that used in England where extension of the patent life is granted if a company is unable to exploit a patented product because of unforeseen events, natural occurrences, government regulations, etc. Industry realizes, however, that it may be almost impossible to change the patent process for pesticides over the near-term, particularly without changing the process for all other proprietary type of products as well.

Industry generally files applications for patents as quickly as possible after some pesticidal activity for a chemical has been demonstrated. Most companies believe that most of the original investment can be returned in the 10 years of useful patent life obtained, assuming a 7-year development time for the pesticide product. Even after the patent has expired, the fact that the development effort, testing, and production facilities have probably been written off, the experience and know-how gained in producing the product, as well as the marketing position achieved, makes it difficult for other companies to competitively price the same product and obtain a significant market share quickly. Although many companies stress the importance of patents and have large patent staffs, they are more concerned about their ability to get particular products registrered than they are to assure an extra amount of patent life for their products.

The trend in some companies recently has been to try to obtain a patent at an "optimum time," i.e., at a time early enough to protect the product yet keep as long a patent life as possible. We expect this trend to continue particularly in view for the requirements for publication of product names and formulas in the Federal Register during the experimental permit process and the availability of data under the 3(c)(1)(D) provision. All of the companies which we contacted indicated that they had not been significantly hurt by patent problems in the past and did not expect to be in the near future.

Originally we had believed that a number of patents issued during a certain time period would be a good indication of innovative activity in the pesticide industry. A review of number of patents issued over a 15-year period indicated no consistent trends. There were several consecutive years in which large numbers of patents were issued and many years in which a relatively modest and constant number were issued. From our discussions with industry and patent attorneys we conclude that some of the variations observed were indicative of patent policies, changes in the Patent Office, the manner in which classes of patents are issued, etc., and not a measure of the innovative activity. Furthermore, it was a general consensus of industry that many patents are filed as defensive measures, that is, paper patents to prevent other companies from patenting the same or similar compounds even though the effectiveness or usefulness of the product has not yet been determined. Patent protection at this early research stage is another measure of insurance for the major pesticide companies. We obtained several examples from industry which indicated that in a particular year's period only a few products were registered, but a large number of patent applications were filed. This trend continues and suggests the protective nature of many patent applications. A portion of industry feels that present patents are becoming more and more narrow in their coverage. As a result companies are having to rely more on developing a strong production and marketing position rather than relying as much as in the past on patent protection.

One area in which additional patent protection is needed is biological controls. A common concern of those few industries pursuing this area of pesticide research is that they cannot obtain patent protection for a proprietary product. Several people believe that patents will eventually be useful in biological control applications, primarily for techniques of formulation, methods of preservation, or means of distribution, instead of patents on the basic pesticide material, bacteria, virus, etc., which are not possible. Process patents will also be obtained but most people do not feel that these will be too valuable.

In summary, industry has more concern that the market share and profitability of a particular product will decrease because of the entrance of new competitive products than concern over the loss of a year in the available patent life as a result of extension of the R&D process.

5. Pesticides for Minor Crop Uses

Of particular concern to the EPA, the public, agriculture and to industry is the possible reduction of the number of pesticides registered for use on minor crops. This reduction has been brought about by legislative action to some extent, because of the increased costs of obtaining registration for a product whether it is registered for a minor or major use. The data requirements for pesticide registration for major and minor uses are similar, i.e., toxicological data, residue data, field testing, carcinogenicity, etc. As a result the costs of the R&D process for minor crop products may not be significantly different from those for major crop products. There will be a difference in development effort required because of the more competitive nature of the market for pesticides for major crops. However, because of the much smaller market for the pesticide for minor crops, the return on investment is significantly less. The minimum "market size" for a product ranges from about $500,000 for a small pesticide company to a $100 million market, with a 10% profit, for larger companies. Industry pursues those chemicals more vigorously which have potential application to major crops such as corn, soybeans, wheat, small grains, etc. The decision is made primarily on the basis of economics. If there is a sufficient market for a product to return the R&D investment and make a reasonable profit for a specific company, there is considerable incentive to develop that product. Both profitability and volume must be combined in making this decision. Once a product is registered for a major crop, there are incentives to extend its registration to minor crops: (1) for public relations and to place the company into a preferred position for selling its products to the major market, (2) because most of the work in environmental fate and toxicity may already have been accomplished and thus only limited residue and other studies need to be done for the minor crop, (3) it is beneficial and economical to capitalize on available plant production, marketing efforts and distribution channels for a product already developed.

Several companies adopt the philosophy that if it will be "easy" to obtain the registration for a particular pesticide, the company will pursue the product even though it may be a minor crop use. Most larger companies believe that three to five uses, i.e., three to five minor crops, would be necessary to support the development of a pesticide used only on minor crops. Other companies believe that their "exposure" is greater with pesticides for minor crop use, i.e., they can be easily sued for product performance, their cost for development are almost as large for major crops, and the risk is higher.

A general conclusion is that changes in regulatory action as well as general economic conditions will lead to a decrease of number and availability of pesticides specific to minor crops. Pesticide development for major crops will be extended to minor crop uses where possible. The decisions will be made on a case by case basis by balancing the necessary added investment with the return provided by both the volume of the market and the profitability of the pesticide. One can expect to find chemicals on the shelf which are suitable for minor crops but which will not be developed because of these economic considerations.

Some of the recommendations made by industry to assist in assuring availability of pesticides for minor crops include: states and state laboratories assist in the development of pesticides for minor crop uses, the EPA provides more active support for the development of pesticides for minor crop uses, the IR 4 program be expanded and improved to aid the farmer in increasing the availability of compounds for small crop uses, and that some of the registration requirements, i.e., data requirements for minor crop uses, be dropped so that the cost of registration is decreased.

6. Differences in Impacts Among Small and Large Companies

In previous sections, we have indicated where specific regulations may have different impacts on companies depending upon their size and available resources. Here we will briefly summarize some of these differences and point out specific problems of the smaller companies involved in pesticide research and development.

In general, the impacts of the regulations and their implementation can be better absorbed by the large diversified companies that do pesticide research (divisions of major oil companies or major chemical companies) than by the smaller companies. The factors which lead to this result include:

- The usually greater long-term commitment to pesticide development of the large companies.
- The availability of capital for both R&D and production facilities of the large companies.
- The availability of external resources through other divisions or subsidiaries of the large companies.
- The multi-national approach to R&D and marketing of the larger companies.
- The normally larger mix of products and organization of the marketing activities of the larger companies.

The long-term commitment allows the larger companies to continue a reasonable level of basic R&D and new synthesis and screening work somewhat independent of the needs for expanding and maintaining the current product lines. The availability of capital permits more timely decision-making and plant investments, as well as the ability to take higher risks in developing pesticides that may or may not be winners. The availability of resources from other parts of a large company make it easier to deal with problems of effluent guidelines, plant design and construction, extra loads in analytical or pilot plant facilities, packaging and disposal without resorting to contract assistance or extra staff to meet these demands. The availability of resources in other countries for testing, screening, synthesis as well as ready availability of markets to yield initial return on investment, provided by multi-national companies adds to the stability of the large company and its ability to absorb specific regulatory impacts. Finally the larger mix of products allows more effective use of distributors, experimental farms, marketing information for decision-making, etc., and provides more opportunity to extend the product line by adding new uses to existing products.

The smaller companies that conduct R&D in pesticides have several advantages, which probably do not counter balance the factors mentioned above. It appears that the R&D efforts of the smaller company are more directed or focused and are more innovative. Smaller companies operate with a lower overhead, are willing to accept smaller markets for their products, and are willing to specialize more to some extent (for minor crop use, or for biological controls, as examples). Unfortunately, it is the belief of most people in pesticide research that EPA legislation discriminated against innovative activity. However, recently proposed regulations have stressed the importance of these biological controls. The provisions of the regulations that encourage integrated pest management and biological control approaches are being challenged by the larger, more established companies.

Many of the larger companies feel that the passage of FEPCA is more of an annoyance, another regulatory process that must be dealt with, than a threat to research. They have the long-term commitment and resources to deal with the regulatory problems. The smaller companies cannot afford the added expense and still maintain profitability.

As a result of these differences in impacts, we expect that the major pesticide developers will continue their R&D activities at the present level almost independent of the regulations, although internal shifts in staff, timing, and product emphasis will occur. These companies will pursue the major market areas and major crops and will probably not venture far into innovative pest control approaches. Increased pesticide use, and the slow but steady development of new pesticides will allow these companies to grow to meet new market demands.

Some of the smaller companies will slowly be diverted from a vigorous research posture. Introduction of competitive products, or the forced withdrawal of a product from the market, can impact the small company seriously unless it has sustained an innovative R&D program on new pesticide development. However, the cost of innovative programs is sufficiently large and requires a continuous long-term effort so that research in many small companies will probably give way to the need to maintain the existing product line and register new crop uses. Thus, in time, some of the small companies may be forced out of the business of innovative research and may become only producers and formulators. Those small companies that have learned to specialize in particular product areas, and that have directed their R&D efforts to well known and established markets, will probably be able to maintain a sufficient flow of new proprietary products to achieve financial success. We expect that these companies will be essential to providing innovative approaches to pest control, and recommend that attempts be made to encourage and support their R&D efforts.

Considering new entries into the pesticide research field, we expect few new entries, not as many as there will be dropouts of both small and large companies. One reason for the lack of new entries is that it requires a minimum of about 10 years of investment, before any product can be brought to registration, and hence marketing. There are few companies willing to make this type of investment in a highly regulated, highly risky business. New entries will most likely result from joint ventures with foreign companies already in the business elsewhere, where a substantive base of R&D and marketing already exists, or from expansion of companies such as the pharmaceutical companies, who are experienced in a regulated industry, and have many of the requisite skills in chemistry, biology, needed facilities, and capital. The trends for moving into the herbicide business from insecticide business will probably continue, because of the larger markets and greater volume of products. Several of the larger companies we contacted indicated that their managements would, under today's conditions, be opposed to their new entry into the pesticide business, primarily because of the greater opportunities for growth and return on investment in other sectors of the chemical business. Most major chemical and oil companies will continue to avoid the biological control area because of the risk involved, the unfamiliarity with the products, the general small volume of production, and other desire to remain a chemical company. The innovative work in this area will probably be left to smaller companies and federally supported efforts.

7. Differences in Responses Among Industry Staff

During this program, we discussed the impact of current regulations on pesticide research and development with several different categories of industry staff--those involved in pesticide research, marketing, management, regulatory liaison, and finance. Although many comments from these diverse representatives were similar in nature and viewpoint, and to some extent represented a company or industry-wide position, some differences in their response was noted.

Those involved in corporate management and finance were specifically concerned with the increased cost and development time that might result from FEPCA implementation. Increased cost and development time could significantly affect the risk, rate of return, and profitability of the pesticide segment of the corporation. This in turn could change its internal competitive position with relation to other parts of the corporation, and affect managements' decisions on the viability of the pesticide segment and their commitment of resources and other support to this segment. Corporate and financial management staff were equally concerned with other EPA regulations--water, air and solid waste--and OSHA regulations and their effect on the future of pesticide business.

Marketing specialists were specifically concerned with the time increases in the registration process and the lack of awareness of seasonal effects in the industry. Delay of one or more growing seasons in the registration of a new product or use of an old product was of importance because of the implications on the marketing organization and the loss of competitive advantage over other companies. The classification system for restricted use pesticides, and certification of applicators, were mentioned by marketing staff as significant sections of FEPCA which affect pesticide markets and have a secondary impact on R&D. The experimental use permit program as first proposed by EPA was criticized heavily by marketing staff because of their previous practice of obtaining much of the efficacy and acceptance data needed to develop marketing strategy from a somewhat loosely controlled experimental permit program.

Research and development staff generally felt that FEPCA implementation did not have a direct impact on the level of work they conducted. However, they felt that implementation of FEPCA would reduce the emphasis and support resources made available to them to do innovative work--to develop new innovative pest control approaches. Their efforts would be expanded in additional test work, support of existing registrations, and other defensive research. As a result, the opportunities to develop, and ultimately market, new pesticides would be significantly reduced. Research and development staff are becoming more aware of concerns of marketing and management staff, since the reduction of resources will affect the direction of their efforts.

8. Biological Control Approaches

In Chaper III the current trends in R&D activity in biological control approaches was discussed. It was pointed out that the major pesticide developers are not pursuing active R&D programs for most biological control approaches, other than plant or insect growth regulators and juvenile hormones (the 'synthetic' biological controls) because of a variety of reasons, most of which have little to do with legislative or regulatory action. There are, however, some positive and negative impacts of the regulations on R&D activities in biological controls which should be mentioned.

Those who are active in the development of biological control approaches, primarily BT, viruses, pheromones, etc., feel that some of the data requirements for registration are unreasonable. They point out that, in some cases, very small amounts of these materials are used in practical application, yet larger quantities must be synthesized and produced only for the tests required for registration, i.e., toxicity, residue, environmental degradation, etc. With the small amounts used, environmental effects, in some cases, become meaningless. Developers believe that a reduced set of test requirements are needed for biological control approaches. (We understand that guidelines for the registration of biological controls are being established.) Of course, those who develop conventional pesticides believe that biological control products should be subjected to the same tests and examined with even more caution because of the general lack of knowledge on their behavior.

As mentioned earlier, there are no direct patent benefits for bacteria or viruses used as pesticide. Industry hopes that section 3(c)(1)(D) can be used to some degree to provide a type of protection to those who develop data needed for registration of biological control pesticides.

The limitations imposed by experimental use permits are believed by industry to restrict R&D in biological control approaches. Large land areas may be needed for effective testing of biological control methods, and several companies feel that this will not be possible under the new experimental use permit system.

The problem of delays, serial data demands, etc., are all mentioned as effects of the current regulations which impact biological control R&D, but technical problems still occupy most of the efforts of the developers.

It is the feeling of those who promote biological controls, that although the law recognizes that these types of innovative approaches should be encouraged, the regulations to date do not encourage their development. However, even if there were special provisions of the regulations to encourage the development of biological controls, it is doubtful that many more companies would participate actively in this R&D effort because of the acceptance, economic, and risk factors mentioned in Section III. Most likely biological control approaches will have to be government supported and/or subsidized within industry to make reasonable progress in today's economic climate.

E. BENEFITS

Most of the discussion so far has focused on negative impacts of the changes in legislation. Positive impacts will occur also, both in regard to R&D and in regard to society in general. Some of the benefits to R&D are as follows:

1. The increase data requirements and the resulting increase in cost have led to a reduction in the number of compounds being put through the R&D process. This in turn has led to a more efficient selection of compounds chosen as potentially successful. Earlier decision making, with increased input from a variety of research areas, decreases risk by decreasing the number of compounds being put through the extensive testing necessary for registration.

2. The need to improve the success to failure ratio also increases the emphasis placed on the directed approach to synthesis and screening, i.e., screening compounds specifically synthesized for pesticidal activity. While presently this approach concentrates on compounds related to existing pesticides, it will allow opportunity for basic biochemical research to direct the synthesis, and thus the development of innovative pesticides based on new modes of action.

3. Ten years ago, the regulatory liaison personnel had to maintain contact with two agencies - FDA and USDA and also anticipate the comments from the Department of Interior and the Department of Health, Education and Welfare. One of the benefits of FEPCA is that present legislation necessitates liaison with only one agency.

4. The increase in data requirements has resulted in better analysis and test methods used for analysis. This increase in sophistication in methods and equipment has resulted in better data and a better understanding of both the mechanisms of pesticide action and the environmental and safety effects of pesticide products.

5. Ultimately the increased amount of data which will be used by EPA to make decisions in registrations, will result in better decisions balancing efficacy and environmental and safety impact and an overall decrease in adverse environmental impact.

6. The certified applicator program will result in two beneficial impacts. First, there will be an elimination of "overkill" in the application of pesticide, i.e., the practice by individual farmers of applying more pesticide than the label recommends in order to assure efficacy. This practice is not as widespread now as in previous years during the introduction of many new pesticides on the market. Additionally, there will be a general upgrading of knowledge concerning the proper use of pesticides by certified applicators and by the state organizations which must certify them. State knowledge of pesticide use and its effects will also increase greatly in those states which accept responsibility for the registration of pesticides.

V. RECOMMENDATIONS TO REDUCE ADVERSE EFFECTS OF FEPCA IMPLEMENTATION

In our discussions with representatives of the pesticide industry, a number of specific recommendations were presented to us on methods by which adverse impacts of FEPCA implementation could be mitigated. Some of these involved specific changes to the regulations which have been proposed and published in the Federal Register; other involved general procedural approaches which EPA could follow, and still others dealt with incentives that could be offered to promote research and development activities. In addition, we have developed some recommendations based upon information received from industry contacts, our review of the literature, and data on the research and development activities of industry. We do not believe it is appropriate to report all the comments provided by industry in response to publications in the Federal Register on specific proposed regulations. These are a matter of public record. Rather we will present briefly a series of recommendations relating to procedures and policies, research activities and incentives programs to be considered by EPA which may expedite and encourage research and development activities by industry and promote the development of safe, effective and environmentally acceptable pesticides.

Procedures and Policies

- Policies and procedures for enhancing the registration/review process at EPA should be considered including:
    - Publish complete guidelines for registration applicants, including definitive test requirements, acceptable test procedures, criteria for acceptance of data, acceptable levels of safety and environmental impact, etc. The guidelines must be sufficiently flexible to cover all products and uses, including biological control and other innovative approaches, and have specific procedures for registration for pesticide mixtures, amendments to labeling, new crop additions, etc.
    - Develop procedures for updating registration guidelines at defined intervals with advance or concurrent notification of potential registrants of any changes between updates.
    - Announce and adhere to definitive schedules for the registration review process, with provisions for scheduled periodic (or interim) formal and informal communications with the registrant to convey additional information or requirements, to discuss results, and promote timely resubmissions, if required. Review schedules should consider the seasonal nature of research and development activities as well as pesticide marketing.

- Modify the procedures for submission of information under Section 3(c)(1)(D) to make it more relevant to the specific company situations.

- Develop procedures to promote internal consistency in the review process in terms of data acceptability, communications, comments, etc. with individual reviewers able to communicate questions of the applicant as soon as they are raised.

- Policies and procedures be considered for expanding and diversifying the EPA Pesticide Registration Staff including:

  - Increase GS ratings and pay levels to provide for advancement of existing staff and recruitment of new staff experienced in agriculture, pesticide development, health and safety, biological controls, and environmental effects.

  - Develop programs for internship/work/study of selected registration division staff at USDA, universities, and industry to gain experience in all phases of the pesticide research development process.

  - Develop an EPA/industry/university interchange program to provide and gain special expertise in diverse fields needed in the registration process, such as biological controls, etc.

  - Provide for flexibility in number and experience of registration staff in periods of seasonal load.

- Policies and procedures be considered for improving intra- and interagency communication, liaison and cooperation including:

  - Increased interaction between OPP Criteria and Evaluation Division and Registration Division.

  - Increased interaction, information exchange and use of staff in EPA regional offices.

  - Increased interaction with USDA research staff to stimulate needed research.

  - Increased interaction and liaison with state environmental and health agencies, pesticide control boards, etc., to enhance states ability to issue experimental permits, certify applicators and register pesticides for local use, to control disposal of containers, etc., and to provide for uniformity among state programs.

- Policies and procedures be considered for enhancing the utility and ease of implementation of experimental use permit and similar limited use programs, including:
    - Use of registration division staff for periodic monitoring of field programs under experimental use permit system.
    - Adopt a co-minitor program for evaluation and monitoring of field studies using registration branch and regional office staff.
    - Develop an alternative approach to the current experimental use permit system which allows for limited sale of pesticides under provisional registration, possibly requiring application by certified applicators, with sufficient restrictions to insure public safety and environmental protection, with submission of data to EPA during the provisional registration period before full registration is granted.
    - Develop an approach whereby distributors and dealers can participate in any experimental use permit system.

Research Activities

- Conduct cost/benefit analyses relating to decisions and criteria for acceptance of toxicity and environmental impact data for product registration, suspension, and cancellation of pesticides.
- Conduct basic biochemical studies to elucidate mechanisms of pest control and enhance the development of new approaches to pest control.
- Develop approaches to improve consumer acceptance of biological control methods.
- Conduct research on interaction of synergism in pesticide mixtures to determine the requirements for tests on mixtures.
- Conduct research on methods of pesticide and container disposal.
- Support basic research in biological control mechanisms, including stabilization of viruses and biological methods of application, isolation, purification, etc.
- Support research on pesticides for use with minor crops.
- Support research on toxicology and environmental effects related to classes of chemicals and biologicals in common use and expected development.

Incentive Programs

- Develop programs of incentives for industry, and universities, to stimulate and encourage research and development on:
    - Innovative pest control methods
    - Pesticides for minor uses

  These incentives programs might include: patents or other protection for bacterial or viral strains, loan system for specific research and development steps with payback provisions, purchase of crops for destruction in field tests.

- Develop internal incentives for EPA staff to adhere to registration schedules, policies and practice and to encourage registration of safe and effective pesticides.
- Consider incentives for complete pest control programs and the total service concept for agriculture.

VI. CONCLUSIONS

The major conclusions developed in this study are:

1. Over the past 25 years, pesticide regulations have increased slowly and steadily in breadth and depth; their impact on innovative research and development in industry has increased in parallel. Major impacts on research and development activities occurred in 1966-1967 as a result of the requirements for finite tolerances and in 1970 as a result of additional environmental data requirements. Implementation of FEPCA will result in additional impacts on specific portions of the R&D process, but will not result in drastic changes in innovative activity. Legislation and regulations have an impact on R&D; the procedural aspects of implementation of these regulations have a major impact on the total pesticide development process.

2. The principal impacts of the steady growth in regulatory action on pesticide research and development activities are:

- a substantial increase in the time required for development of a pesticide from synthesis through registration
- a substantial increase in the cost to develop and register individual pesticides
- an increased quantity and quality of data on the use, application, safety and environmental effects of pesticides
- increased risk for the developer because of uncertainty of the timing and extent of return on the R&D investment
- increased allocation of R&D resources to the defense and maintenance of existing product lines and extension of pesticides to new uses at the expense of decrease in innovative R&D
- a reordering of the timing of specific R&D activities and reallocation of some R&D manpower resources
- increased use of outside resources to conduct portions of the R&D process for the pesticide industry
- increased emphasis on products which involve foreign markets in order to increase volume sales

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3. The principal aspects of the implementation of FEPCA which will have the most effect on pesticide R&D are continued increases in environmental data requirements and their uncertainty, and the implementation of the experimental use permit system. Increased R&D costs, lengthening and reordering of the R&D tasks, and shifts of resources to extending product lines are the most important changes anticipated. Only minor impacts on R&D activities are anticipated from regulatory provisions dealing with certified applicators, restricted use designation, rights to data and compensation for data, packaging, disposal, etc.

4. The principal impacts of pesticide regulation on future pesticide products are:

- continued development of herbicides and other potentially high volume/profit compounds
- continued emphasis on products for major agricultural crops with decreasing emphasis on products for minor crops
- continued decrease in the number of new pesticide compounds which enter the marketplace, resulting from increased costs per compound in the development phase.

5. The principal decision-making factors in the R&D process for proceeding with the development of a specific pesticide are, in order of importance: efficacy, projected cost compared to competitive products, anticipated sales volume and profitability, human safety (toxicity), and environmental impact. Although the recent regulations may eventually increase the importance of environmental impact as a decision-making factor, the other factors remain more important in determining which potential products will reach the marketplace.

6. The large established multi-product diversified pesticide developer will continue to be the major source of R&D effort in industry, and will continue to develop and market new products with minimum impact of regulations. The smaller and more recently formed companies, which have only few viable products to use as a basis for research commitment, may not be able to sustain the increases in R&D costs and extended product development time. They will either withdraw from the R&D function, be consolidated with larger companies, or withdraw from the marketplace. Increased costs from regulatory action will hasten this process. Unfortunately many of the smaller and more recently formed companies have a greater capacity and ability for innovative research than other firms since they are less chemically oriented and less oriented toward large volume sales.